Ultrasound Evaluation of Intima-Media Thickness of Carotid Arteries in Adults with Primary Hypertension at Ibadan, Nigeria

Evaluation échographique de l'épaisseur de l'intima-Media des artères carotides d'adultes avec une *hypertension essentielle à Ibadan, Nigeria*

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ABSTRACT

BACKGROUND: **Ultrasound measured Carotid Intima-Media Thickness (CIMT) is a simple and inexpensive tool for assessing the cumulative effects of hypertension on the carotid arterial walls. It is also an independent predictor of future myocardial infarctionand stroke risk.**

OBJECTIVES: **This study compared ultrasound measured CIMT in hypertensive adults with non-smoking normotensive controls. It also documented variations in CIMT with subjects' age and sex.**

METHODOLOGY: **Hypertensives (120) of both sexes aged 18years and above were recruited from the Hypertension Clinic at University College Hospital (UCH) Ibadan. Normotensive controls (120) were also recruited from the general public. The CIMT was measured on B- mode ultrasound using the technique of 'Multiple Carotid Sites Measurement'**

RESULTS: **Mean CIMT values were 0.756mm ± 0.130 and 0.751mm ± 0.129 for the hypertensive group and 0.638mm ± 0.088 and 0.670mm ± 0.107 for the control group on the left and right sides respectively (P=0.000). Higher CIMT values were noted among male hypertensive subjects (P=0.030). CIMT values also showed positive correlation with subjects' age.**

CONCLUSION: **There was a significant difference in CIMT for hypertensives when compared with normotensives in the study area. CIMT also varies with subjects' age and sex. WAJM 2013; 32(1): 62–67.**

Keywords: **Ultrasound,carotid, intima-media thickness, hypertension.**

RÉSUMÉ

CONTEXTE: La mesure échographique de l'épaisseur Intima-Media de la Carotide (EIMC) est un examen simple, non coûteux pour l'évaluation de l'effet cumulé de l'hypertension sur la paroi de l'artére carotide. C'est aussi un prédicteur indépendant d'un infarctus futur du myocarde et de risque d'AVC.

Objectifs: Cetteétude comparait l'EIMC chez des adultes hypertendus acec celle de témoins normotendus non fumeurs. Elle a aussi documenté les variations d'EIMC selon l'âge et le sexe des patients.

Méthodologie: Des patients Hypertendus (120) des 2 sexes, âgés de 18 ans et plus étaient recrutés à partir de la consultation d'hypertendus de l'Hôpital Universitaire d'Ibadan. Des témoins normotendus (120) ont été recrutés à partir de la population générale. L'EIMC a été mesurée par échographie en mode B en utilisant la technique de 'Mesure sur Sites Multiples de la Carotide'

Résultats: Les valeurs moyennes d'EIMC étaient de 0,756mm ± 0,130 et 0,751mm ± 0,129 pour le groupe d'hypertendus et de 0,638mm ± 0,088 et 0,670mm ± 0,107 pour le groupe des témoins sur les côtés gauches et droits respectivement (P=0.000). Des valeurs plus élevées d'EIMC étaient notés chez les hommes (P=0.030). Les valeurs d'EIMC montraient aussi une corrélation positive avec l'âge des patients.

Conclusion:

Il y'avait une différence significative d'EIMC chez les hypertendus comparés aux normotendus dans cette population d'étude. L'EIMC variait selon l'âge et le sexe des sujets. **WAJM 2013; 32(1): 62–67.**

Mots clés: **Echographie, carotide, épaisseur intima-média, hypertension**

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Abbreviations: **BP,** Blood Pressure; **CIMT,** Carotid Intima-Media Thickness; **HT,** Hypertension; **IMT,** Intima-Media Thickness; **UCH,** University College Hospital, **US,** Ultrasound;

INTRODUCTION

High blood pressure, also referred to as hypertension (HT) is defined as a blood pressure (BP) reading of 140/90mmHg or above on three consecutive measurements done at least six hours apart.[1] Hypertension is classified as primary (essential) or secondary but primary hypertension is responsible for the vast majority of diagnosed cases and heredity is the most important known factor in its development.[1, 2] Primary Hypertension is also strongly associated with lifestyle including such habits as smoking and alcohol consumption while secondary hypertension is caused by a pre-existing medical condition such as renal disease, diabetes and other malfunctions of the endocrine system.[1] Akinkugbe[3] (1972) put the prevalence of hypertension in the adult African population at 10–15%. Also, a survey by the 1997 expert committee on non-communicable diseases in Nigeria reported prevalence of hypertension in adult Nigerians aged 15 years and above, to be 17–20%.[4]

Hypertension is a common cardiovascular problem and a major public health burden in both developed and developing countries; it is also the dominant risk factor for stroke in Nigeria[5]. Persistently high blood pressure causes the heart to work harder than it should and can damage the coronary arteries, the brain, the kidneys and the eyes. Prolonged hypertension is characterized by adaptive changes which result in thickening of arterial walls and it is also a risk factor for the development of atherosclerosis by various mechanisms.[6] High-resolution B-mode Ultrasound (US) is a non-invasive, simple, safe, inexpensive, precise and reproducible method which is able to evaluate and characterise such adaptive vascular changes such as arterial wall thickening and atherosclerotic progression. Ultrasound permits accurate quantification of the intima-media thickness (IMT), which is a measurement of the thickness of the artery walls. Studies have shown some correlation between carotid intima-media thickness (CIMT) and hypertension.[6–9] CIMT has also been shown to correlate with cardiac risk factors and it is an independent predictor for the future risk for myocardial .... [6, 7] It has been reported that CIMT has an early predictive value for organ damage[6, 7] and it acts as a tool for the detection of sub-clinical atherosclerosis which helps clinicians to more effectively identify the vulnerable patient who will benefit from aggressive preventive intervention. However, there is paucity of information on the role of quantification of CIMT by ultrasound in hypertensive patients in the study area.

The aim of this study is to evaluate the CIMT in hypertensive adults using B-Mode Ultrasound and compare with CIMT in non-smoking adults (controls) with normal blood pressure (normotensive) in the study area. It is postulated that the results of this study will assist clinicians to better predict the likelihood of end organ damage in hypertensive patients and guide the management of such patients.

SUBJECTS, MATERIALS AND METHODS

This is a prospective, case-control study conducted at the Department of Radiology of the UCH Ibadan, Nigeria between January and May 2011. A total of 240 individuals comprising 120 hypertensive adult subjects and 120 non-smoking normotensive adult volunteers were recruited into this study.

The Convenience Sampling method was usedand participants were selected from patients presenting for consultation at the hypertension clinic at the UCH Ibadan. The sample size was calculated using the 'Difference of Means' formula. Informed consent was obtained from all participants. Ethical approval was obtained from the Ethical Committee and Institutional Review Board of the University of Ibadan/ University College Hospital.

Subjects' age and sex were documented. Their first, second and third consecutive blood pressure measurements were noted from medical records to support hypertensive status.

Inclusion Criteria

Individuals of either sex diagnosed with primary hypertension, aged 18 years and above were included in the study. Persons with complications due to hypertension involving organs like the heart, kidneys or brain were also included in the study. The control group were normotensive, non-smoking individuals recruited from the general population. They were also aged 18years and above with an age distribution similar to the hypertensive cases and with no known history or symptoms of diabetes mellitus.

Exclusion Criteria

Hypertensives aged less than 18 years or who were pregnant were excluded from this study. Normotensive individuals with a known history or symptoms of diabetes mellitus, previous history of vasculitis or symptoms suggestive of pathology of vascular origin were also excluded as controls for this study.

Ultrasound Technique

Ultrasound examination of the carotid arteries was performed using a 7.5–10MHz linear transducer on a Logic-P5 General Electric ultrasound machine. The intima-media thickness (IMT) was measured using the technique of 'Multiple Carotid Sites Measurement'.[10] Avoiding plaques, the CIMT of the far walls of the carotid arteries were taken at the following sites bilaterally on a longitudinal scan plane: (i) about 1.5cm proximal to the carotid bulb (ii) at the carotid bulb and (iii) at the proximal internal carotid arteries (ICA).

To obtain an optimal image, the sound waves were beamed perpendicularly to the arteries to show the two parallel echogenic lines which correspond to the lumen-intima and media-adventitia interfaces. The IMT is the distance between the leading edge of the first bright line on the far wall (lumen-intima interface) and the leading edge of the second bright line (media-adventitia interface) –Figure 1. The final IMT was the average of the 3 values at the three sites examined on each side.

Statistical analysis of the data was done using SPSS Software version 17.0 for Windows. Associations between categorical variables were explored with the Chi-Square test, while numeric variables were compared with the Student T-test. Associations were deemed significant if P-value <0.05.

RESULTS

There were 240 subjects comprised of 120 hypertensive cases with an age range of 21–80years and 120 normotensive control subjects with an age range of 20–69 years. The mean age for the cases was 50.6 years ± 10.9, while the mean age for the controls was 47.7 years ± 12.1. The mean age difference for the two groups is not statistically significant (p value = 0.055). Of the 240 subjects, 190 (79.2%) were above the age of 40years, with the largest proportion (39%) being in the 50–59 years age bracket (Table 1). Majority (72.5%) of subjects in the control group were above the age of 40 years, with the largest proportion (50.8%) within the 50–59 years age bracket. Similarly, majority (85.8%) of the hypertensive cases were above the age of 40years, but the largest proportion (32.5%) were within the 40–49 years age bracket.

There was a statistically significant larger proportion of female than male subjects (P=0.021). The male and female sex frequencies were 41.7% and 58.3% for the hypertensives and 27.5% and 72.5% for the controls respectively (Table 2).

The mean CIMT values for the hypertensive cases were significantly higher on both sides when compared with CIMT values in the control cases (P<0.001). The mean right CIMT value was 0.751mm ± 0.129 and 0.670mm ± 0.107 for the case and control groups respectively. On the left, the mean CIMT value was 0.756mm ±0.130 and 0.638mm ±0.088 for the case and control groups respectively (Table 3).

There was a positive correlation between CIMT values bilaterally and the age of the subjects in both groups (Table 4). However, for the hypertensive cases, the correlation was stronger on the left side while it was stronger on the right side in the control group.

The left CIMT was slightly higher than the right for the hypertensive cases; however this difference was not statistically significant. (P=0.069). For the control group, the mean CIMT value on the right side was statistically significantly higher than on the left (Table 5).

Among hypertensive subjects, the mean CIMT value was significantly

Table 1: Frequency Distribution of Age Groups for Cases and Controls

Age Group (years)	Hypertensives (%)	Controls (%)	Total (%)
20 – 29	5(4.2)	19(15.8)	24(10).0
30 – 39	12(10.0)	14(11.7)	26(10.8)
40 – 49	39(32.5)	12(10.0)	51(21.3)
50 – 59	33(27.5)	61(50.8)	94(39.2)
>60	31(25.8)	14(11.7)	45(18.7)
Total	**120(100.0)**	**120(100.0)**	**240(100.0)**

Table 2: Sex Distribution for Cases and Controls

Gender	Cases (N-120)N (%)	Controls (N-120)N (%)	Total N (%)	Chi -Square	P-Value
Male	50(41.7)	33(27.5)	83(34.6)	5.323	0.021
Female	70(58.3)	87(72.5)	157(65.4)		
Total	**120(100.0)**	**120(100.0)**	**240(100.0)**		

Table 3: Mean CIMT* Values in Hypertensives and Controls

Subjects	N	Mean CIMT Value ±SD (mm)	T-Test	P-value
Left				
Hypertensive	120	0.756 ±0.130	8.185	0.000
Control	120	0.638 ±0.088		
Right				
Hypertensive	120	0.751 ±0.129	5.219	0.000
Control	120	0.670 ±0.107		

*CIMT, Carotid Intima Media thickness

Table 4: Correlation between Age and CIMT* for Cases and Controls

Parameter	Left	Right
+PCC Cases	0.520	0.427
P Value	0.000	0.000
+PCC Controls	0.403	0.454
P Value	0.000	0.000

*CIMT, Carotid Intima Media thickness; +PCC, Pearson's Correlation Coefficient

Table 5: Comparison of Mean CIMT* values between the Left and the Right Sides within each Study Group

Subjects	N	Mean CIMT Value ±SD (mm)	T-Test	P-value
Hypertensives				
Left	120	0.756 ±0.130		
Right	120	0.751 ±0.129	0.400	0.069
Controls				
Left	120	0.638 ±0.088		
Right	120	0.670 ±0.107	–3.813	0.000

*CIMT, Carotid Intima Media thickness

Table 6: Comparison of mean CIMT* values between Genders within each Study Group

Subjects	Sex	N	Mean CIMT ± SD (mm)	T-Test	P-Value
Hypertensives					
Right	Male	50	0.781±0.124		
	Female	70	0.729±0.130	2.202	0.030
Left	Male	50	0.779±0.127		
	Female	70	0.740±0.131	1.601	0.112
Controls					
Right	Male	33	0.659±0.099		
	Female	87	0.675±0.111	0.728	0.468
Left	Male	33	0.624±0.078		
	Female	87	0.645±0.091	1.200	0.233

CIMT, Carotid Intima Media thickness

Table 7: Presence of Carotid Plaques in the Hypertensive Cases and Controls

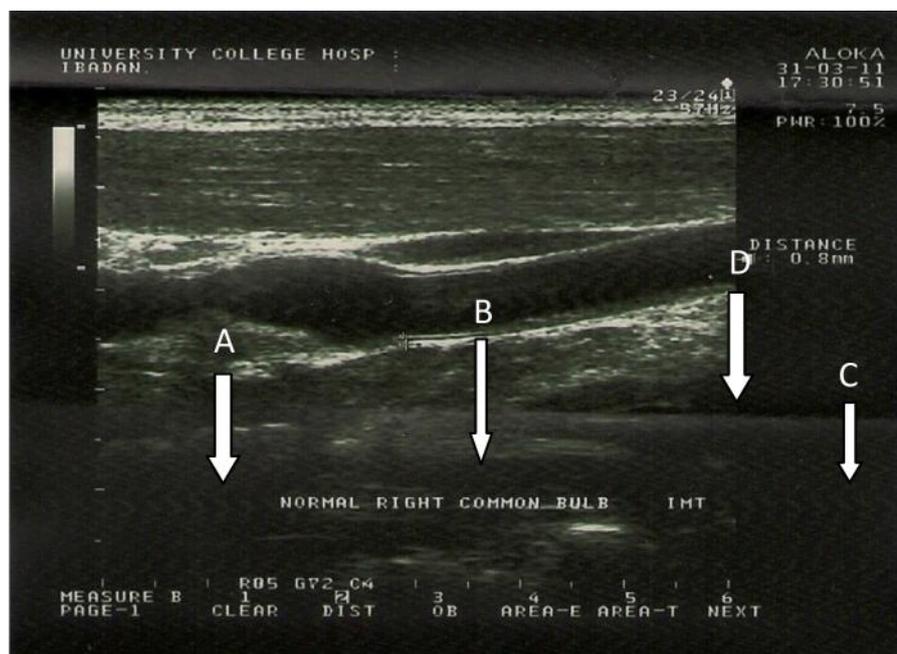| Carotid Plaque	Hypertensives (%)	Controls (%)	Chi Square	P-value
Right				
Present	21(17.5)	18(15.0)		
Absent	99(82.5)	102(85.0)	0.276	0.600
Left				
Present	14(11.7)	9(7.5)		
Absent	106(88.3)	111(92.5)	1.202	0.273

Fig. 1: Longitudinal Scan, B-Mode Ultrasound Image showing how the IMT is measured (Cursors). A: Internal Carotid Artery; B: Carotid Bifurcation; C: Common Carotid Artery; D: Internal Jugular Vein.

higher for males on the right side, while there was no significant difference on the left (Table 6). For the controls however, neither the right nor the left CIMT values varied significantly by gender.

As noted in Table 7, carotid plaques were seen in more hypertensive cases than controls but this difference is not statistically significant.

DISCUSSION

Using B-Mode ultrasound, IMT of large arteries like the carotid arteries which are relatively close to the skin can be measured from outside the body. Intima media thickness (IMT) has increasingly been used in medical research since the mid 1990s to monitor changes in arterial walls.[11] Generally, arterial wall thickening may be in the intima layer or in the muscular media layer. As the carotid artery is an elastic artery, the muscular media is relatively small. Hence, thickening of the carotid arterial wall is essentially due to intima thickening.[11] Normal mean CIMT values of 0.5mm and 0.9mm have been reported for the young (20-30years) and for older (>60years) age groups respectively[10] while values between 0.9–1.4 mm are considered as thickening, with values higher than 1.4mm being indicative of an atheromatous plaque.[12] However since CIMT is a marker of cardiovascular risk, the normal value should be interpreted in terms of increased risk rather than in terms of statistical distribution within a population. A value of CIMT 1mm above the normal range at any age is associated with a significantly increased incidence of myocardial infarction and/or cerebro-vascular disease.[10]

The 120 hypertensive adults in this study have a mean age of 50.61years while the mean age for the 120 controls is 47.73years. Using ultrasound, the mean CIMT for the hypertensive cases is 0.751mm and 0.756mm on the right and the left sides respectively. These values are significantly higher than the mean CIMT in the normotensive control subjects where the mean CIMT values are 0.670mm and 0.638mm on the right and left sides respectively (P<0.001). This finding is in agreement with Schutte *et al*[13] who in a study of young South African men with a mean age of 45.2

and 38.9 years; documented an overall mean CIMT of 0.75mm and 0.61mm (P < 0.01) for the hypertensive and normotensive cohorts respectively. Similarly, in an American population, Kotsis et al[14] reported that hypertensive subjects tended to have higher mean CIMT than normotensive subjects. Findings from these studies corroborate the fact that high blood pressure is a major determinant of CIMT across various races and regions.

A wide range of CIMT values have been recorded for hypertensives by various authors, ranging from 0.762mm to 0.969mm.[6, 15] However, the figures in this study are closest to those of South African men as measured by Schutte et al[13] and this wide difference in CIMT values is probably due to the variations within the study populations in different geographic, economic and cultural settings. Factors such as diet and consumption habits, living standard, lifestyle and health practices ultimately influence individual health status, and these same factors may have a role in the prevalence of hypertension and the global variation in the reported CIMT values.

Freitas et al[7] in Brazil reported thatCIMT correlated positively with age especially after 64 years of age. The present study also showed a statistically significant positive correlation between age and CIMT for the hypertensive cases and other studies have also corroborated this finding.[6, 8, 15]

With regard to gender, the mean CIMT values in male hypertensives were higher bilaterally than in females but this finding was statistically significant only on the right side (P<0.05). However, for the controls there was no statistically significant difference between both sexes. This CIMT variation with gender among the hypertensive group is at variance with reports from some previous studies.[7, 8] Sorof et al[8] in a study of hypertensive adolescents in the United States and Freitas et al[7] in a study of Brazilian hypertensive adults reported that CIMT did not vary significantly by gender. A study with a larger sample size will be required to make a definitive statement on gender variation in CIMT values for the hypertensive population

in this study area. A higher mean CIMT in hypertensive males may however be due to the generally higher prevalence of hypertension among males in our community.[16, 17]

For hypertensive cases in this study, the left mean CIMT (0.756mm) was higher than the right (0.751mm), but this difference is not statistically significant. On the other hand, for the control group the right mean CIMT (0.670mm) was significantly higher than the left (0.638mm, P<0.01). Sharma et al[6] who studied 304 hypertensive subjects in Nepal aged 35–65 years also reported marginally higher CIMT value on the left side (Right: 0.968mm, left: 0.969mm). Luo et al[18] in China reported that bilaterally, CIMT becomes thicker with age ($p<0.01$) and that the left CIMT was significantly thicker compared with the right between the ages of 35 and 65 years (P<0.05). No definite explanation has been proposed for this disparity in CIMT measurements but may be due to the fact that the left common carotid artery is a direct branch of the aorta and thus may experience more direct pressure and flow changes associated with hypertension than the right common carotid artery which arises from the brachiocephalic trunk. Further studies are however required in this area.

A carotid plaque is a focal structure arising from the intima media layer of the arterial wall and encroaches into the arterial lumen. Plaques are produced by intimal lipid deposits and may appear echogenic on ultrasound.[19] In a study of Korean adult subjects, Kwon et al[19] noted that the prevalence of hypertension was significantly higher in patients with carotid plaques. Another study with Asian subjects[20] also reported that the detection risk of carotid plaque increased with the classification of hypertension. This study shows a higher prevalence of carotid plaques among the hypertensive subjects when compared to the controls, however, this difference is not statistically significant.

Conclusion

This study shows a statistically significant increase in CIMT in hypertensive adults when compared with non-smoking normotensive controls in the

study area. This increased CIMT amongst the hypertensive subjects is seen to correlate positively with subjects' age. Higher mean CIMT values are also seen in male hypertensive subjects when compared to females.

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