

# **Original Research Article**

## **Carotid intima-media thickness and risk of cardiovascular disease among healthy adult volunteers in north eastern Nigeria**

### **Abstract**

**Background:** Assessment of carotid intima media thickness (CIMT) have evolved over the years to assume a key role in assessment of cardiovascular risk. It combines the advantages of being sensitive, non-invasive and reproducible test for atherosclerotic vascular disease. We assessed CIMT and its association with cardiovascular risk factors among apparently healthy individuals.

**Methods:** Apparently healthy adults were consecutively recruited from July 2013 through March 2014 at the Federal Medical Centre Nguru. Anthropometric variables were measured and blood samples collected. CIMT was determined at the common carotid, carotid bifurcation, and proximal internal carotid artery levels using a high-resolution 2-D USS scanner. Means of continuous variables were compared using Student t-test or Mann-Whitney *U* test, while between groups mean was compared using one-way ANOVA. Association of CIMT other continuous variable was assessed using bivariate correlation and multivariable linear regression models. A *p* value of <0.05 was considered significant for all statistical analysis.

**Results:** Ninety nine apparently healthy consenting adults comprising 63(63.6%) males and 36(36.4%) females were consecutively recruited. Their median (interquartile range) age was 34(27) years. Mean left CIMT at common carotid, carotid bifurcation and internal carotid artery levels were 0.82(0.22), 0.91(0.23) and 0.85(0.21) respectively( $F=3.57, p=0.029$ ). There was no difference in CIMT between the left and the right sides. Thirty one (31.3%) had CIMT above 0.9mm. Significant correlation was found between CIMT and age ( $r^2=0.33, p<0.001$ ), body mass index(BMI) ( $r^2=0.06, p<0.001$ ), systolic blood pressure ( $r^2=0.11, p=0.001$ ), glycated haemoglobin ( $r^2=0.34, p<0.001$ ), total cholesterol ( $r^2=0.42, p<0.001$ ), LDL-c ( $r^2=0.47, p<0.001$ ) and HDL-c ( $r^2=-0.14, p<0.001$ ). Age, BMI, blood pressures, total cholesterol, LDL-c and HDL-c independently predicted CIMT.

31 **Conclusion:** The prevalence of increased CIMT is high among healthy adults, and CIMT  
32 correlated positively with other cardiovascular risk factors. Routine assessment of CIMT may  
33 identify individuals with increased risk for cardiovascular diseases and result in more targeted  
34 preventive measures.

35 **Keywords:** Carotid-Intima-Media-Thickness; Healthy adults; Cardiovascular Risk.

36

## 37 **Introduction**

38 Cardiovascular disease is an important cause of morbidity and mortality in the developing  
39 world, Nigeria inclusive (1, 2). This has featured prominently as a leading cause non-  
40 communicable disease (NCD) death, followed by malignancies/other neoplasms, respiratory  
41 diseases and diabetes mellitus (2). Although hypertensive heart disease, rheumatic heart  
42 disease (RHD) and dilated cardiomyopathy (DCM) including peripartum cardiomyopathy  
43 (PPCM) remains the dominant aetiologies for heart related death in sub-Saharan Africa, the  
44 region is faced with high burden of atherosclerotic cardiovascular diseases including stroke  
45 and myocardial infarction (3, 4).

46 Assessment of carotid intima media thickness (CIMT) using ultrasound (USS) have evolved  
47 over the years to assume a key role in the assessment of cardiovascular risk (5, 6). It  
48 combines the unparalleled advantages of being a sensitive, non-invasive and a reproducible  
49 test for assessing atherosclerotic vascular diseases and risk of CVD. The predictive and  
50 prognostic roles of CIMT for CVD has been validated in a number of landmark studies (7, 8),  
51 leading to its inclusion in the list of diagnostic tools for global cardiovascular risk assessment  
52 (9). Its impact is mainly in individuals with intermediate 10-year risk for cardiovascular  
53 events, allowing for reclassification to either the low-risk or high-risk category (10). This has  
54 an enormous implication for the implementation of cost effective preventive measures.

55 There are a number of published researches on CIMT from different regions of Nigeria, but  
56 most of the studies centred on subjects with defined cardiovascular risk factors (11-14). We  
57 sought to determine CIMT and its association with other cardiovascular risk factors among  
58 apparently healthy individuals from the northeast sub-region of Nigeria. This, we believe will  
59 add to the scanty pool of information on CIMT among healthy Nigerians, and allow for a  
60 more representative national reference to be generated.

61

## 62 **Methods**

63 Apparently healthy consenting adults from all works of life were consecutively recruited  
64 from July 2013 to March 2014 at the Federal Medical Centre (FMC) Nguru. People with  
65 history or findings consistent with cardiovascular diseases or its treatment, substance abuse as  
66 well as pregnant women were excluded from the study. Anthropometric variables were  
67 measured using standard protocols, and blood samples collected for determination of blood  
68 sugar, cholesterol and BUN. Body mass index (BMI) was classified using the WHO  
69 guideline (15), while cholesterol levels were classified according to the NCTP III guideline  
70 (16). Blood pressure was classified using the JNC 8 guideline (17).

71 Assessment of CIMT was done by a single radiologist with expertise in vascular USS, using a  
72 high-resolution 2-D USS scanner. Carotid USS was performed with the subjects lying supine  
73 and the neck slightly extended. The head was directed away from the side of interest, and  
74 images systematically obtained at the common carotid, carotid bifurcation, and proximal  
75 internal carotid artery levels in both longitudinal and short axis planes. Images of the far wall  
76 of carotid artery was used in assessing CIMT. The intima-media interface was recognised in  
77 zoomed images, and CIMT determined using the leading-edge to leading edge method.  
78 Carotid plaques, where present were classified according to modified Gray-Weale  
79 classification (18).

80 Data was analysed using SPSS software (22.0). Normally distributed continuous variables  
81 were expressed as means (SD), while those not consistent with parametric distribution were  
82 expressed as median (interquartile range). Categorical variables were expressed as  
83 proportions and percentages. Means of continuous variables were compared using Student t-  
84 test or Mann-Whitney *U* test as appropriate, while between groups mean was compared using  
85 one-way ANOVA with Turkey's post-hoc analysis. Paired-sample t-test was used in  
86 comparing CIMT of the right and left side. Categorical variables were compared using  
87 Fischer exact Chi-square test. Association of CIMT other continuous variable was assessed  
88 using bivariate correlation and multivariable linear regression analysis. A *p* value of <0.05  
89 was considered significant for all statistical analysis.

90

91

92

93 **Results**

94 Ninety nine apparently healthy consenting adults comprising 63 (63.6%) males and 36  
95 (36.4%) females were consecutively recruited. Their median (interquartile range) age was  
96 34(27) years. The females are significantly older than the males ( $p<0.001$ ). Their clinical  
97 characteristics are illustrated in table 1.

98 The mean BMI was  $22.1(2.12) \text{ kg/m}^2$ , with 86(86.9%) having normal weight, 4 (4%) being  
99 overweight, and 9 (9.1%) being underweight. Pre-hypertensive systolic blood pressure (SBP)  
100 was documented in 57 (57.6%), while 2(2%) had SBP of 140mm Hg. Twenty one (21.2%)  
101 had a diastolic blood pressure (DBP) of 90mm Hg (with SBP less than 140mm Hg), while 23  
102 (23.2%) had a pre-hypertensive DBP.

103 One (1.3%) subject had a fasting blood glucose of 8.6mmol/L, but none had impaired fasting  
104 glucose. The mean glycated haemoglobin (HbA1c) was 4.8(0.82) %. Total cholesterol was  
105 elevated in 26(26.3%), while elevated low density lipoprotein cholesterol (LDL-c) was  
106 documented in 24 (24.2%). Ten (10.1%), comprising of two males and eight females had low  
107 levels of high density lipoprotein cholesterol (HDL-c).

108 The mean right and left CIMT were 0.84(0.25) mm and 0.85(0.24) mm at the common  
109 carotid artery ( $p=0.456$ ), 0.93(0.26) mm and 0.94(0.25)mm at the carotid bifurcation  
110 ( $p=0.567$ ), and 0.86(0.23)mm and 0.86(0.24)mm at the internal carotid ( $p=0.712$ )  
111 respectively. However, CIMT differed at the various levels ( $F=3.57$ ,  $p=0.029$ ), being highest  
112 at the level of carotid bifurcation. Males and females had comparable CIMT at all levels.  
113 However, there was a significant difference in mean CIMT between the various age groups  
114 ( $F=12.92$ ,  $p<0.001$ ). Individuals in the age groups 45 years and above had a significantly  
115 higher CIMT at similar levels than those 44 years and below in whom measured CIMT were  
116 also similar (table 2). Subjects with SBP of 120mm Hg and above, glycated haemoglobin  
117 greater than 6% and total cholesterol greater than 5.2mmol/L had significantly higher CIMT  
118 (table 3). Thirty one (31.3%) of the subjects had CIMT above 0.9mm.

119 Significant correlation was found between left internal carotid artery CIMT and age ( $r^2=0.33$ ,  
120  $p<0.001$ ), BMI ( $r^2=0.06$ ,  $p<0.001$ ), SBP ( $r^2=0.11$ ,  $p=0.001$ ), HbA1c ( $r^2=0.34$ ,  $p<0.001$ ), total  
121 cholesterol ( $r^2=0.42$ ,  $p<0.001$ ), LDL-c ( $r^2=0.47$ ,  $p<0.001$ ) and HDL-c ( $r^2=-0.14$ ,  $p<0.001$ ).  
122 Using a threshold of 0.9mm (table 4), individuals having higher left internal carotid artery  
123 CIMT had significantly increased age ( $p<0.001$ ), SBP ( $p<0.001$ ), DBP ( $p=0.003$ ), BMI  
124 ( $p<0.001$ ), HbA1c ( $p<0.001$ ), total cholesterol ( $p<0.001$ ), LDL-c ( $p<0.001$ ) and lower

HDL-c ( $p<0.001$ ). Age, BMI, blood pressures, total cholesterol, LDL-c and HDL-c independently predicted CIMT (table 5).

## **Discussions**

This is the first time CIMT is being evaluated among apparently healthy adults aged 18 years and above in north-eastern part of Nigeria. The average CIMT in our study is comparable to what was reported in Jos (11), although their subjects were relatively older. Even though our female cohorts were significantly older than the males, there was no difference in CIMT between the two groups, a finding in contrast with reports from other parts of the world.

Similar to what was earlier reported from north-central Nigeria (11), our measured CIMT is higher than what was documented from other regions of the world (19-21). Whether this is indicative of higher CIMT among apparently healthy Nigerians compared to Caucasians will require a larger, multi-centre study to establish. The atherosclerosis in communities (ARIC) and the multi-ethnic study of atherosclerosis (MESA) study reported comparable CIMT in Caucasians and African-Americans (22, 23). Most of the recent studies employed the use of semi-automated quantitative edge detection technique for measuring CIMT as opposed to the manual method used in our study. However, the manual method has been validated to have comparable reproducibility to the semi-automated method (24). In addition to variation in technique, differences in burden of atherosclerotic risk factors, sample size as well as ethnic and geographic diversity might also contribute to the observed differences in measured CIMT. Blacks are known to have higher blood pressures and left ventricular mass compared to Caucasians. Whether these differences in cardiovascular profile applies to CIMT remains to be established.

The high prevalence of traditional cardiovascular risk factors among the apparently healthy subjects studied might be responsible for the high prevalence of increased mean CIMT observed. This has reflected in the significant correlations observed between the various atherosclerotic risk factors and CIMT. Several studies had previously established the roles of these various atherosclerotic risk factors in the development of vasculopathy (25, 26). Many of the traditional risk factors independently predicted CIMT, a finding similar to what was previously reported (7, 8). The rather weak predictive value of age ( $r^2=0.33$ ,  $p=0.048$ ) in our study might be explained by the fact that the 62 (62.6%) of the subjects studied were younger than 45 years.

Measurement of carotid intima-media thickness is increasingly becoming a valuable tool in assessing cardiovascular risk factors by providing information beyond that provided by traditional risk factors. This is particularly important in the setting of intermediate cardiovascular risk where CIMT may result in reclassification into either higher or lower risk category, allowing for a more cost-effective management of patients. The atherosclerosis risk in communities (ARIC) study showed an increase in risk for coronary heart disease of 17% in men and 38% in women for every 0.19mm increase in CIMT over a follow-up period ranging from 4 to 7 years (27). The risk for stroke and myocardial infarction were similarly reported to increase by up to 28% for every 0.20mm increase in CIMT over 6 years of follow-up (23). Our study is not designed or powered to determine whether the increased CIMT in our apparently healthy cohorts translates into higher cardiovascular event rate. There are no studies on the prognostic implications of increased CIMT among Nigerians.

The findings of increased CIMT as well as the high prevalence of traditional cardiovascular risk factors among our apparently healthy subjects has important implication. There is the need to assess these factors in a community wide study so that the looming epidemic of cardiovascular diseases can be averted. In addition, larger cohorts devoid of cardiovascular risk factors will be required to establish normal CIMT in our population.

Our study has a few limitations. Most of the subjects are younger than 45 years of age with fewer proportions of females, making comparison with other studies difficult. Because of the substantial number that are not eligible for assessment of risk using the Framingham risk score, we were unable to assess its association with CIMT. All CIMT measurement were carried out one radiologist and intra-observer variability was not established. Finally, we used manual method for measuring CIMT, rather than the semi-automated edge detection method.

Table 1: Clinical characteristics of the participants

| Variable                 | Male (n=63) | Female (n=36) | <i>p</i>            |
|--------------------------|-------------|---------------|---------------------|
| Age (years)              | 29 (24)*    | 45.5(29)*     | <0.001 <sup>†</sup> |
| BMI (kg/m <sup>2</sup> ) | 21.6(2.07)  | 22.79(2.02)   | 0.008               |
| Blood pressure (mmHg)    |             |               |                     |
| Systolic                 | 114.9(8.96) | 120.8(10.79)  | 0.004               |
| Diastolic                | 72.9(9.91)  | 78.6(9.61)    | 0.006               |
| FBS (mmol/l)             | 4.5(0.79)   | 4.3(0.50)     | 0.118               |

|     |                            |            |            |       |
|-----|----------------------------|------------|------------|-------|
| 189 | HbA1c (%)                  | 4.8(0.83)  | 5.0(0.78)  | 0.187 |
| 190 | Total cholesterol (mmol/l) | 4.1(1.11)  | 4.7(0.98)  | 0.002 |
| 191 | LDL-c (mmol/l)             | 2.8(0.81)  | 3.2(0.81)  | 0.012 |
| 192 | HDL-c (mmol/l)             | 1.7(0.46)  | 1.6(0.47)  | 0.296 |
| 193 | Triglycerides (mmol/l)     | 2.1(0.28)  | 2.2(0.35)  | 0.340 |
| 194 | Intima-media thickness     |            |            |       |
| 195 | Right CC                   | 0.81(0.24) | 0.90(0.27) | 0.068 |
| 196 | Left CC                    | 0.82(0.22) | 0.90(0.27) | 0.135 |
| 197 | Right CB                   | 0.90(0.25) | 0.98(0.28) | 0.117 |
| 198 | Left CB                    | 0.91(0.23) | 0.98(0.28) | 0.152 |
| 199 | Right ICA                  | 0.85(0.22) | 0.88(0.26) | 0.443 |
| 200 | Left ICA                   | 0.85(0.21) | 0.89(0.28) | 0.431 |

201 BMI=Body mass index; FBS=Fasting blood sugar; HbA1c=Glycated haemoglobin; LDL-  
 202 c=Low density lipoprotein cholesterol; HDL-c=High density lipoprotein cholesterol;  
 203 CC=Common carotid; CB= carotid bifurcation; ICA=Internal carotid artery; \*=Median  
 204 (interquartile range); †=Mann-Whitney U test

205

206 Table 2: Mean left internal carotid intima-media thickness by age group

|     |           |            |                |
|-----|-----------|------------|----------------|
| 207 | Age group | Number (%) | Mean CIMT (mm) |
| 208 | <24       | 30(30.3)   | 0.78(0.106)    |
| 209 | 25 – 34   | 20(20.2)   | 0.69(0.189)    |
| 210 | 35 – 44   | 12(12.1)   | 0.775(0.277)   |
| 211 | 45 – 54   | 17(17.2)   | 1.053(0.223)   |
| 212 | 55 – 64   | 14(14.1)   | 1.056(0.201)   |
| 213 | >64       | 6(6.1)     | 1.050(0.105)   |

214 CIMT=Carotid intima-media thickness

215

216

Table 3: Comparison of left internal carotid intima-media thickness based on levels of various cardiovascular risk factors

| Variable                   | CIMT (mm)  | <i>P</i>  |
|----------------------------|------------|-----------|
| SBP (mmHg)                 |            | 0.032     |
| $\geq 120$                 | 0.91(0.23) |           |
| $< 120$                    | 0.80(0.23) |           |
| DBP (mmHg)                 |            | 0.111     |
| $\geq 80$                  | 0.91(0.26) |           |
| $< 80$                     | 0.83(0.21) |           |
| FBS (mmol/l)               |            | 0.457     |
| $> 5.6$                    | 0.86(0.24) |           |
| $\leq 5.6$                 | 0.95(0.24) |           |
| HbA1c (%)                  |            | $< 0.001$ |
| $> 6.0$                    | 1.08(0.17) |           |
| $\leq 6.0$                 | 0.83(0.23) |           |
| Total cholesterol (mmol/l) |            | $< 0.001$ |
| $> 5.2$                    | 1.16(0.11) |           |
| $\leq 5.2$                 | 0.75(0.17) |           |
| LDL-c (mmol/l)             |            | $< 0.001$ |
| $> 4.0$                    | 1.74(0.07) |           |
| $\leq 4.0$                 | 0.79(0.20) |           |
| Triglyceride (mmol/l)      |            | 0.464     |
| $\geq 1.7$                 | 0.87(0.24) |           |
| $< 1.7$                    | 0.66(0.13) |           |

CIMT=Carotid intima-media thickness; SBP=systolic blood pressure; DBP=diastolic blood pressure; FBS=fasting blood sugar; HbA1c=glycated haemoglobin; LDL-c=low density lipoprotein cholesterol.

Table 4: Comparison of cardiovascular risk factors based on left internal carotid intima-media thickness

| Variable                   | Left CIMT (mm) |              | <i>P</i> |
|----------------------------|----------------|--------------|----------|
|                            | >0.9 (n=31)    | ≤0.9 (n=68)  |          |
| Age (years)                | 53.74(9.95)    | 30.24(11.51) | <0.001   |
| SBP (mmHg)                 | 122.26(8.84)   | 114.71(9.69) | <0.001   |
| DBP (mmHg)                 | 79.35(8.14)    | 72.44(10.38) | 0.003    |
| BMI (kg/m <sup>2</sup> )   | 23.32(1.05)    | 21.48(2.24)  | <0.001   |
| FBS (mmol/l)               | 4.60(0.49)     | 4.13(0.96)   | 0.001    |
| HbA1c (%)                  | 5.67(0.58)     | 4.46(0.60)   | <0.001   |
| Total cholesterol (mmol/l) | 5.62(0.63)     | 3.70(0.68)   | <0.001   |
| LDL-c (mmol/l)             | 3.95(0.65)     | 2.45(0.35)   | <0.001   |
| HDL-c (mmol/l)             | 1.33(0.32)     | 1.75(0.46)   | <0.001   |
| Triglycerides (mmol/l)     | 2.14(0.28)     | 2.16(0.32)   | 0.762    |

CIMT=Carotid intima-media thickness; SBP=systolic blood pressure; DBP=diastolic blood pressure; BMI=body mass index; FBS=fasting blood sugar; HbA1c=glycated haemoglobin; LDL-c=low density lipoprotein cholesterol.

Table 5: Association of some risk factors with intima-media thickness in multivariable regression analysis

|                          | Standardised $\beta$ | 95% CI          | <i>p</i> |
|--------------------------|----------------------|-----------------|----------|
| $R^2=0.67$               |                      |                 |          |
| Age                      | 0.210                | 0.000 – 0.006   | 0.006    |
| BMI                      | -0.411               | -0.065 - -0.027 | <0.001   |
| Systolic blood pressure  | 0.401                | 0.005 – 0.014   | <0.001   |
| Diastolic blood pressure | -0.378               | -0.013 - -0.005 | <0.001   |
| Fasting blood glucose    | 0.117                | -0.017 – 0.096  | 0.172    |
| HbA1c                    | 0.003                | -0.056 – 0.057  | 0.975    |
| Total cholesterol        | 0.376                | 0.015 – 0.145   | 0.017    |
| LDL-c                    | 0.435                | 0.052 – 0.194   | 0.001    |
| HDL-c                    | -0.173               | -0.165 - -0.012 | 0.023    |
| Triglyceride             | 0.106                | -0.015 – 0.177  | 0.098    |

BMI=Body mass index; HbA1c=Glycated haemoglobin; LDL-c=Low density lipoprotein cholesterol; HDL-c=High density lipoprotein cholesterol

# **References:**

1. Mensah GA. Ischaemic heart disease in Africa. *Heart*. 2008;94(7):836-43.
2. Dalal S, Jose Beunza J, Volmink J, Adebamowo C, Bajunirwe F, Njelekela M, et al. Non-communicable diseases in sub-Saharan Africa: what we know now. *International Journal of Epidemiology*. 2011;40(4):885-901.
3. Mensah GA, Roth GA, Sampson UKA, Moran AE, Feigin VL, Forouzanfar MH, et al. Mortality from cardiovascular diseases in sub-Saharan Africa, 1990-2013: a systematic analysis of data from the Global Burden of Disease Study 2013. *Cardiovascular Journal of Africa*. 2015;26(2):S6-S10.
4. Roth GA, Forouzanfar MH, Moran AE, Barber R, Nguyen G, Feigin VL, et al. Demographic and Epidemiologic Drivers of Global Cardiovascular Mortality. *New England Journal of Medicine*. 2015;372(14):1333-41.
5. Lorenz MW, Sitzer M, Markus HS, Bots ML, Rosvall M. Prediction of clinical cardiovascular events with carotid intima-media thickness: A systematic review and meta-analysis - Response. *Circulation*. 2007;116(9):E318-E.
6. Prati P, Tositto A, Vanuzzo D, Bader G, Casaroli M, Canciani L, et al. Carotid intima media thickness and plaques can predict the occurrence of ischemic cerebrovascular events. *Stroke*. 2008;39(9):2470-6.
7. Sehestedt T, Jeppesen J, Hansen TW, Wachtell K, Ibsen H, Torp-Pedersen C, et al. Risk prediction is improved by adding markers of subclinical organ damage to SCORE (vol 31, pg 883, 2010). *European Heart Journal*. 2010;31(13):1662-.
8. Nambi V, Chambless L, Folsom AR, He M, Hu Y, Mosley T, et al. Carotid Intima-Media Thickness and Presence or Absence of Plaque Improves Prediction of Coronary Heart Disease Risk The ARIC (Atherosclerosis Risk In Communities) Study. *Journal of the American College of Cardiology*. 2010;55(15):1600-7.
9. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germanof G, et al. 2007 ESH-ESC practice guidelines for the management of arterial hypertension - ESH-ESC task force on the management of arterial hypertension. *Journal of Hypertension*. 2007;25(9):1751-62.
10. Peters SAE, den Ruijter HM, Bots ML, Moons KGM. Improvements in risk stratification for the occurrence of cardiovascular disease by imaging subclinical atherosclerosis: a systematic review. *Heart*. 2012;98(3):177-84.
11. Okeahialam BN, Alonge BA, Pam SD, Puepet FH. Carotid intima media thickness as a measure of cardiovascular disease burden in nigerian africans with hypertension and diabetes mellitus. *International journal of vascular medicine*. 2011;2011:327171-.
12. Ayoola OO, Onuwaje MA, Akintomide AO. Sonographic assessment of the carotid intima-media thickness on B-mode ultrasonography in a Nigerian population. *Nigerian medical journal : journal of the Nigeria Medical Association*. 2015;56(5):357-61.
13. Owolabi MO, Agunloye AM, Umeh EO, Akpa OM. Can common carotid intima media thickness serve as an indicator of both cardiovascular phenotype and risk among black Africans? *European Journal of Preventive Cardiology*. 2015;22(11):1442-51.

14. Akintunde AA, Adebayo PB, Aremu AA, Opadijo OG. Carotid atherosclerosis and right ventricular diastolic dysfunction in a sample of hypertensive Nigerian patients. *Croatian Medical Journal*. 2013;54(6):555-60.
15. Eveleth PB. Physical status: The use and interpretation of anthropometry. Report of a WHO Expert Committee - WHO. *American Journal of Human Biology*. 1996;8(6):786-7.
16. Morgan JM, Capuzzi DM. Hypercholesterolemia - The NCEP adult treatment panel III guidelines. *Geriatrics*. 2003;58(8):33-8.
17. Abel N, Contino K, Jain N, Grewal N, Grand E, Hagans I, et al. Eighth joint national committee (JNC-8) guidelines and the outpatient management of hypertension in the African-American population. *North American Journal of Medical Sciences*. 2015;7(10):438-45.
18. Geroulakos G, Ramaswami G, Nicolaides A, James K, Labropoulos N, Belcaro G, et al. CHARACTERIZATION OF SYMPTOMATIC AND ASYMPTOMATIC CAROTID PLAQUES USING HIGH-RESOLUTION REAL-TIME ULTRASONOGRAPHY. *British Journal of Surgery*. 1993;80(10):1274-7.
19. Sun Y, Lin CH, Lu CJ, Yip PK, Chen RC. Carotid atherosclerosis, intima media thickness and risk factors-an analysis of 1781 asymptomatic subjects in Taiwan. *Atherosclerosis*. 2002;164(1):89-94.
20. Youn YJ, Lee NS, Kim J-Y, Lee J-W, Sung J-K, Ahn S-G, et al. Normative Values and Correlates of Mean Common Carotid Intima-Media Thickness in the Korean Rural Middle-aged Population: The Atherosclerosis Risk of Rural Areas in Korea General Population (ARIRANG) Study. *Journal of Korean Medical Science*. 2011;26(3):365-71.
21. Mannami T, Konishi M, Baba S, Nishi N, Terao A. Prevalence of asymptomatic carotid atherosclerotic lesions detected by high-resolution ultrasonography and its relation to cardiovascular risk factors in the general population of a Japanese city - The Suita study. *Stroke*. 1997;28(3):518-25.
22. Howard G, Sharrett AR, Heiss G, Evans GW, Chambless LE, Riley WA, et al. CAROTID-ARTERY INTIMAL-MEDIAL THICKNESS DISTRIBUTION IN GENERAL POPULATIONS AS EVALUATED BY B-MODE ULTRASOUND. *Stroke*. 1993;24(9):1297-304.
23. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK, Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. *New England Journal of Medicine*. 1999;340(1):14-22.
24. StenslandBugge E, Bona KH, Joakimsen O. Reproducibility of ultrasonographically determined intima-media thickness is dependent on arterial wall thickness - The Tromso study. *Stroke*. 1997;28(10):1972-80.
25. Glass CK, Witztum JL. Atherosclerosis: The road ahead. *Cell*. 2001;104(4):503-16.
26. Stamler J, Neaton JD, Wentworth DN. BLOOD PRESSURE SYSTOLIC AND DIASTOLIC AND RISK OF FATAL CORONARY HEART DISEASE. *Hypertension (Dallas)*. 1989;13(5 SUPPL. 1):I2-I12.
27. Chambless LE, Heiss G, Folsom AR, Rosamond W, Szklo M, Sharrett AR, et al. Association of Coronary Heart Disease incidence with carotid arterial wall thickness and major risk factors: The Atherosclerosis Risk in Communities (ARIC) Study, 1987-1993. *American Journal of Epidemiology*. 1997;146(6):483-94.