**NORMAL FEMORAL ARTERY INTIMA-MEDIA THICKNESS AMONG HEALTHY NIGERIAN ADULTS; RELATIONSHIP WITH AGE, GENDER AND BODY MASS INDEX**

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**Sources of Grant/Support**: None.

**Conflict of Interest**: None

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**ABSTRACT**

**Background**: Ultrasonographic intima media thickness is now the imaging modality of choice for the clinical evaluation of large arterial wall thickening (atherosclerosis). It is a proven simple, reliable, accurate, reproducible, affordable and ionizing radiation-free marker of atherosclerosis. Carotid intima media thickness (IMT) values have been widely employed as a surrogate marker of atherosclerosis; normal values have been documented for Nigerians and values above the nomogram are regarded as evidence of atherosclerosis. However, recent scientific evidence shows that the femoral artery intima-media thickness is a better indicator of atherosclerosis, compared to the IMT of the carotid artery. Despite the femoral IMT being a better indicator of atherosclerosis, there is paucity of data on femoral intima media thickness among healthy Nigerian adults.

**Objective**: To determine the femoral IMT among a healthy, normotensive, normoglycemic adult Nigerian cohort, and its relationship with age, sex and body mass index among the study population.

**Materials and Methods:** This was a hospital-based cross-sectional study among a cohort of normotensive, non-diabetic adult healthy volunteers. The socio-demographic characteristics, anthropometric and clinical parameters, as well as the B-mode ultrasonographic IMT of both common femoral arteries were evaluated. The data was analysed using IBM SPSS version 23.0. The student t-test and One-way-ANOVA were used to test the association between age, sex and FIMT as appropriate. The correlations between the FIMT and age and BMI were assessed by Pearson’s correlation coefficients; linear regression analysis was done to determine the equation relating FIMT to factors with significant correlation coefficients among the subjects. p values <0.05 were taken as statistically significant.

**Results**: A total of 106 femoral arteries in 53 individuals were evaluated in this preliminary study. The mean age was 50.7(SD14.4) years (range 27-77 years). Twenty-eight (52.8%) were males and 25 (47.2%) were females. The mean Femoral Intima Media Thickness (FIMT) for the whole group was 0.53(SD0.05) mm. The FIMT in males, 0.54(SD0.05) mm was not significantly different from that in females, 0.52(SD0.06) mm (p= 0.221**)**. The mean left FIMT, 0.54(SD0.05) mm was significantly higher than the right FIMT, 0.52(SD0.06) mm (p<0.001**)**

There was a significant positive Pearson correlation coefficient between FIMT and age, (r=0.719, p<0.001). The linear regression equation was FIMT = 0.39 + 0.003\*Age (years) indicating a mean increase of 0.003 mm in FIMT for every one-year increase in age.

There was no significant correlation between BMI and FIMT, (r=0.008, p=0.952).

**Conclusion**: The overall mean FIMT among a cohort of South-West Nigerian adults without cardiovascular risk factors was 0.53(0.05) mm. The mean FIMT in males was not significantly different from that in females, but the mean FIMT on the left was significantly higher than that on the right. There was a significant positive correlation between FIMT and age, with an increase in FIMT of 0.003mm for every one-year increase in age. There was no correlation between FIMT and BMI. Screening FIMT may help in the early discovery of increased IMT, which would be of value in re-classification of cardiovascular risk.

**Keywords**: Femoral artery, Ultrasonography, Atherosclerosis, Intima media thickness.

**Introduction**

Ultrasonographic intima media thickness has emerged as the imaging modality of choice in the clinical evaluation of large arterial wall thickening (atherosclerosis). It has also been validated as a simple but reliable and accurate, reproducible, affordable and ionizing radiation-free marker of atherosclerosis, among other imaging modalities.1

Atherosclerosis, a chronic inflammatory disease of the arteries principally initiated by accumulation of low-density lipoprotein, remnant lipoprotein particles and active inflammatory process in focal areas of arteries2, is a major public health epidemic with enormous burden on the population.3

A major sequalae of atherosclerosis is atherosclerotic cardiovascular disease (ACD) which mainly lead to ischemic heart disease (IHD) and cerebrovascular disease (mainly ischemic stroke). ACD remains the leading cause of mortality worldwide with IHD and stroke, both complications of ACD, the world’s first and third leading causes of death, respectively.1

Although atherosclerosis is a generalized disease process, the extent of atherosclerosis and its effects differ in different vascular beds.4 In some affected vessels, the atherosclerotic disease is limited to the vascular intima with measurable intima thickening of the wall, as seen in the carotid arteries5, the aorta and its branches.6 In other arteries, it may also result largely from media layer thickening, as demonstrated in the femoral arteries.5 Generally, the large artery intima-media thickness has been adopted as an indicator of the total individual burden of arteriosclerosis.7

The ultrasonographic measurement of IMT, especially of the carotid artery has been widely adopted as a marker of atherosclerosis. Over the years, the carotid artery intima-media thickness (CIMT) has become an established surrogate marker of atherosclerosis with scientifically proven, documented association with cardiovascular risk factors and outcomes.8,9 There is also scientific evidence from clinical and epidemiological studies that CIMT values >0.9mm are associated with adverse cardiovascular events.10

Recently Simon et al, however, reported that an isolated common carotid artery intima-media thickness measurement may be an inadequate parameter for generalized atherosclerosis.11 Adams et al12 in their study found a poor correlation between carotid intima-media thickness alone and the extent and severity of atherosclerosis.

Current emerging scientific evidence8,13,14,15,16,17, however, has shown that the femoral artery is a better arterial site to assess generalized atherosclerosis and its measurement alone or in combination with the carotid artery IMT is a far better indicator of atherosclerosis. Other studies have also shown that atherosclerosis is found to be more advanced in the femoral arteries, when measured simultaneously with the carotid arteries.16,17 Furthermore, the incorporation of intima-media thickness from femoral and carotid arteries together yielded better correlation with cardiovascular risk factors than the CIMT alone8. Also, Kirhmajer et al14 found a positive correlation between femoral artery intima-media thickness and cardiovascular risk factors such as high and low-density lipoprotein, body mass index, smoking and male gender. They reported femoral artery intima-media thickness as a novel marker of cardiovascular risk factors.14 This was further corroborated by a study by Wang and colleagues15, where it was concluded that increased femoral artery intima-media thickness cross sectional area has a significant association with the male gender, age older than 35 years and body mass index greater than 30 kg/m2.

There is now a shift to early detection of subclinical arterial damage for cardiovascular risk assessment and to identify subjects with increased risk who may benefit from certain preventive measures10, and establishing reference values of normal intima media thickness are crucial to the detection of abnormal arterial thickness.

Previous studies by Ayoola et al18 reported a FIMT of 0.6mm in healthy adults, while Depairon et al19 in a study among healthy subjects between ages of 20 and 60, also reported FIMT of 0.543 ± 0.063 in women and 0.562mm ±0.074 in men. In addition, positive correlation between age and femoral intimal media thickness have been recorded in healthy population.9 Ogeng’o et al20 also reported a progressive increase of the femoral intima media thickness with age.

Apart from age that affects IMT generally, Ethnicity and inter geographic variations in IMT have been established by previous studies12, hence the use of refence values from other parts of the World may be inappropriate in detecting pathological thickness in our environment.

Despite the emerging evidence that the femoral artery intima-media thickness is a better indicator of atherosclerosis, than the intima-media thickness of the carotid artery21, there is a paucity of data on the femoral intima media thickness normal values among healthy Nigerian adults.

In this preliminary study, we therefore determined the FIMT among healthy, normotensive, non-diabetic, normal body mass index subjects, in our environment. This will help to detect arterial thickening early in individuals at risk of cardiovascular events, help institute prompt management to prevent adverse cardiovascular events.

**Materials and Methods**

This was a prospective, cross-sectional study carried out between January and June

2016. The study was conducted in the Department of Radiology, of a major tertiary hospital with 850 beds located in South-Western Nigeria. The Radiology department provides services for inpatients and out-patients.

The Sample size was calculated using the formula: N = (Z2\*sd2)/d2

Z = 1.96 for 95%, SD = 0.07 (standard deviation on mean FIMT. (Depairon et al. 200019) d = 0.02 (precision). Hence N = 47.1. Accounting for 10% attrition,

 N = 47.1/0.9 = 52.3, Sample size = 53

Fifty-three (53) male and female normotensive, non-diabetic, normal body mass index adult healthy volunteers of all ages from the General outpatients’ department of the hospital, selected by systematic sampling method were enrolled after approval of the study by the UI/UCH ethics committee with approval number UI/EC/15/040. The inclusion criteria were being normotensive, normoglycemic, and having normal lipid profile and body mass index. Subjects with a history of or on medication for cardiovascular disease, deranged lipid profile was excluded from his study.

All recruited consenting healthy adult volunteers had their sociodemographic recorded. Their anthropometric parameters: weight and height were measured with a bathroom weighing scale and a stadiometer respectively, and recorded in a prepared data form. The blood pressure of all recruited subjects was recorded after a 15 minutes rest, using a mercury sphygmomanometer.

About 5 mls of venous blood was taken for fasting blood glucose and fasting lipid profile estimation. Patients with fasting blood sugar between 70–110 mg/dl, total cholesterol of <200 mg/dl, triglycerides of <150-200 mg/dl, low-density lipoprotein 80–120 mg/dl, and high-density lipoprotein of 35–86 mg/dl as well as blood pressure less than 140/90 mmHg and normal BMI were recruited into this study.

**Ultrasound evaluation**

B-mode ultrasonographic measurement of the femoral intima media thickness was done by the same observer, using Ultrasonix SonixSP ultrasound machine with a 7.5-10MHz transducer. The procedure was adequately explained to the patients and consent was taken. The subjects were positioned supine for the examination. The thigh was adequately exposed and flexed at the hip and knee and the thigh was externally rotated. The patient was draped and the acoustic gel was applied to the skin of the thigh to minimize the air interface between the probe and skin. The scanning of both common femoral arteries was done from just above the inguinal ligament to its bifurcation into profunda femoris and superficial femoral branches. The intima-media thickness was measured thrice as the leading edges of lumen intima interface and of the media adventitia interface at a point 1-2cm proximal to the bifurcation of common femoral arteries and the mean was recorded.22-24 This measurement was done at the far wall because of the near wall’s gain dependency and unreliability.25 Presence of plaques within the vessels, distinct area of localized thickness with an intima-media thickness more than 1.5mm26, were also recorded. The flexed thigh and knee were returned to the normal position after the procedure and the acoustic coupling gel was completely wiped off after the examination. The total scanning time was about 10 minutes on the average.

**Data Analysis**

Data was entered and analyzed using IBM SPSS version 23.0. The results of clinical data and arterial measurements of the study population were displayed as mean (+/- standard deviation, SD) or as percentages. The student t-test was used to compare numeric variables; for more than two groups ANOVA was used and if this showed significant difference the Games-Howell post-hoc analysis was used to determine where the differences actually lay. The correlations between the FIMT and age and BMI were assessed by Pearson’s correlation coefficients; linear regression analysis was done to determine the equation relating FIMT to factors with significant correlation coefficients among the subjects. Differences were considered significant if p<0.05.

**RESULTS**

A total of 53 healthy adult participants were enrolled. There were twenty-eight (52.8%) males and twenty-five females. The mean age of the participants was 50.7(SD14.4) years with a range of 27 to 77 years. Subjects aged between 41 to 60 years formed the largest group. There were no significant differences, between males and females, in their demographic characteristics (Table 1).

In addition, there were no significant differences, between males and females, in their anthropometric parameters and the mean systolic and diastolic blood pressures (Table 2).

In table 3, B-mode ultrasonographic measurement of common femoral artery IMT showed a mean for the whole group of 0.53(0.05) mm. The FIMT for the males, 0.54(SD0.05) mm was not significantly different from that for the females, 0.52(SD0.06) mm (p=0.221). The FIMT on the left, 0.54(SD0.05), was significantly higher than that on the right, 0.52(SD0.06) mm using paired t-test (p<0.001).

There was significant difference in the mean FIMT between the various age groups (F (2,25.8) = 25.843; p<0.001). Post hoc tests showed that the mean FIMT of participants aged 40 years and below, 0.49(SD0.02) mm) was significantly lower than the mean FIMT of participants aged 41 to 60 years, 0.52(SD0.04) mm) (p=0.014) and that of participants >60 years old, 0.59(SD0.06) mm (p<0.001). Likewise, the mean FIMT of participants aged 41 to 60 years was significantly lower than the mean FIMT of participants aged above 60 years (p<0.001) (Table 4). This is confirmed by the significant positive Pearson correlation coefficient between FIMT and age, r=0.719, p<0.001. The linear regression equation was FIMT = 0.39 + 0.003\*Age (years) (Figure 1a) indicating a mean increase of 0.003 mm in FIMT for every one-year increase in age.

There was no significant correlation between BMI and FIMT, r=0.008, p=0.952 (Figure 1b).

Evaluation for femoral artery plaques in the study population, showed the presence of plaques in 9 out of the fifty-three (17%) healthy participants studied. All plaques were seen in participants older than 60 years of age with a mean FIMT of 0.61(SD0.06).

**Discussion**

The intima-media thickness of large arteries like the common carotid and common femoral arteries is a measure of atherosclerotic changes.1

The FIMT is less affected by cardiac cycle variations27, more reliable as cardiac cycle variation induced the femoral artery variability does not reach the threshold for statistical significance28,29 in addition to the fact that FIMTs are more reproducible, compared to CIMT.27,28

However, unlike the carotid arteries, there is a paucity of data on femoral artery IMT reference values among the healthy adult population in our environment. This preliminary study showed a mean femoral intima-media thickness of 0.53(SD0.05) mm in a healthy population with a mean age of 50.7(SD14.4) years, lower than the 0.6mm documented by Ayoola et al., in Ile-Ife Nigeria 18, but slightly higher than the 0.49(SD0.09) mm reported by Layne et al29 in a study conducted among a younger population with a mean age of 32.0(SD1.2) years in the United States. However, Ogeng’o et al20, in their work among two hundred and eight adult black Kenyans with a mean age 36.4 years who had died of trauma, reported a mean femoral intimal media thickness of 0.76(SD0.016) mm, which is notably higher than the findings from our current study. In the study by Ogeng’o et al20, the femoral intimal media thickness was measured postmortem by histology. This difference in methodology might have been responsible for the observed difference. In a study in Brazil, Godoi et al. reported mean FIMT of 0.74(SD0.3) mm in healthy controls30, while Lucatelli et al. also reported 0.73 mm as median FIMT in a study among Italians with no cardiovascular disease.31 The differences in mean FIMT values may differ due to ethnic differences and geographical variations.12

Although the mean intimal media thickness in this index study was slightly higher in males than in females, this was not statistically significant. This observation is in agreement with findings by Depairon et al19 in a study to determine the reference values of carotid and femoral intima-medial thickness for age and gender in healthy subjects aged 20 to 60, with no family or personal history of cardiovascular disease or atherogenic risk factors, using ultrasound. They reported a mean femoral intimal media thickness of 0.543(SD0.063) mm in women and 0.562(SD0.074) mm in men, but the difference was not statistically significant. In contrast, Ogeng’o et al20, reported a significantly higher mean femoral intimal media thickness in males, 0.815(SD0.012) mm than in females, 0.712(SD0.015) (p = 0.023). 20

Previous studies have reported a positive correlation between age and femoral intimal media thickness in a healthy population.16,31 Between the ages of 20 and 60, Depairon et al19 reported that the femoral intima-media thickness increased by 1.2 microns per year (not statistically significant) in women but by 3.1 microns/year (p < 0.002) in men. Ogeng’o et al20 also reported a progressive increase in femoral intima-media thickness with age such that it was 0.69(SD0.014) mm in those under 30 years and 0.94(SD0.03) mm in those over 70 years, the difference being statistically significant (p=0.031). This index study also corroborates previous findings that age influences intima-media thickness in healthy adults with a significant increase in the mean FIMT observed in subjects among various age groups. Another study among normotensive patients by Plavnik et al. found a positive correlation between FIMT and age (r = 0.44, p<0.0005).26

No significant relationship between BMI and FIMT was observed in this study, in contrast to the findings of the French AXA study conducted among participants with cardiovascular risk factors, including age32 and also corroborated by the works of Cheng et al.9 Those two studies found a significant association between FIMT and BMI. The fact that the present study was among participants without cardiovascular risk factors, enrolling only individuals with normal BMIs could explain the observed difference between the findings of those studies and the present study.

Besides, our result showed that the FIMT on the left was significantly higher than that on the right, in tandem with the findings of Kollias and colleagues that the left side femoral IMT was higher and more closely related to cardiovascular risk factors (mainly systolic BP) than that on the right side in children33. Several other studies also corroborated the fact that IMT is higher on the left side than the right side in middle-aged or older populations.34,35,36 The higher FIMTs on the left may suggest that atherosclerotic changes are seen earlier in the left femoral arteries compared to the right. It is alsointerestingto note that all the femoral plaques were in participants older than 60 years, which corroborates the findings of several researchers who reported that peripheral arterial disease increases with age.37,38,39

In this study, the reference values in healthy individuals without cardiovascular risk factors without and with femoral artery plaques were 0.53(SD0.05) mm and 0.61(SD0.06) mm, respectively, in our environment.

Though the carotid IMT screening is employed more commonly as a proven tool in the re-categorization of patients earlier grouped as intermediate cardiovascular risk into mild or high-risk categories40,41,42, FIMT is equally of clinical value in intermediate cardiovascular risk patients.43,44 The fact that atherosclerosis occurs earlier in the femoral arteries17, may mean FIMT values above the observed average normal values may be of more clinical relevance in early re-categorization of patients with intermediate cardiovascular risks.

There is a need to have reference values for normal FIMT, in order to detect increased or abnormal FIMT values in our population. The commonly used description for increased IMTs include IMT greater than the 75th percentile, IMT at the upper quartile or IMT at the upper tertile, an absolute value (for example  ≥0.9 mm or ≥1 mm in the carotid arteries), 75th percentile for age, ethnicity, and sex and IMT that is >1 SD above the mean.45,46 Although absolute value for FIMT is not widely available, in this study, the mean FIMT values (SD) were evaluated. Values higher than 1 SD of FIMTs with or without plaques may indicate increased IMT and atherosclerotic changes in our environment.

**Limitations of the study**

Although the intima-media complex thickness measurements are known to be reproducible, the single observer that performed the scan in this study has made inter-observer variation assessment impossible. The sample size employed may limit extrapolation to a larger population. Further population-based study with a larger sample size is advocated in the future.

**Conclusion**

The overall mean FIMT among a cohort of South-West Nigerian adults without cardiovascular risk factors was 0.53(0.05) mm. The mean FIMT in males was not significantly different from that in females, but the mean FIMT on the left was significantly higher than that on the right. There was a significant positive correlation between FIMT and age, with an increase in FIMT of 0.003mm for every one-year increase in age. There was no correlation between FIMT and BMI. Screening FIMT may help in the early discovery of increased IMT, which would be of value in re-classification of cardiovascular risk and ultimately guide treatment.

**Acknowledgment**

We acknowledge the cooperation and participation of the resident doctors of the Department of Radiology and also thank the staff of the ultrasound suite of the University College Hospital, Ibadan.

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**Table 1: Sociodemographic Characteristic of the Study Population**

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| --- | --- | --- | --- |
| **Variables**  | **Male (%)** | **Female (%)** | **p-value** |
| Age (years) Below 40 41 to 60 Above 60 | 9 (32.1)13 (46.4)6 (21.4) | 8 (32.0)10 (40.0)7 (28.0) | 0.836 |
| Occupation  Artisan Civil servant Teaching Trading Retired Unemployed |  2 (7.10)8 (28.6)4 (14.3)7 (25.0)6 (21.4)1 (3.60) | 4 (16.0)2 (8.00)2 (8.00)9 (36.0)5 (20.0)3 (12.0) | 0.313 |
| Education  Uneducated Primary  Secondary Tertiary | 2 (7.10)4 (14.3)4 (14.3)18 (64.3) | 7 (28.0)3 (12.0)7 (28.0)8 (32.0) | 0.060 |
| Tribe Hausa Igbo Yoruba | 1 (3.60)0 (0.00)27 (96.4) | 1 (4.00)3 (12.0)21 (84.0) |  |

**Table 2: Anthropometric and Blood Pressure Values Among the Healthy study cohort**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  VARIABLES | MALES Mean (SD) | FEMALESMean (SD) | TOTAL Mean (SD) | P-Value |
| Systolic blood pressure (mmHg) | 122(11.3) | 123(9.77) | 123(10.5) | 0.825 |
| Diastolic blood pressure (mmHg) | 78.0(8.70) | 75.2(8.59) | 76.7(8.69) | 0.233 |
| Weight (Kg) | 66.7(7.82) | 70.5(8.00) | 68.5(8.06) | 0.084 |
| Height (m) | 1.68(0.07) | 1.69(0.07) | 1.69(0.07) | 0.547 |
| BMI (Kg/m2) | 23.5(1.90) | 24.3(2.13) | 23.8(2.02) | 0.072 |

**Table 3: Ultrasonographic Femoral Intimal Thickness Measurements in the study cohort**

|  |  |  |  |
| --- | --- | --- | --- |
| **VARIABLES** |  | **TOTAL** | **p-value** |
| **MALES**  | **FEMALES** |
|  | **Mean(SD) mm** | **Mean(SD) mm** | **Mean(SD) mm** |
| Right FIMT | 0.52(0.05) | 0.51(0.06) | 0.52(0.06)**@** | 0.407 |
| Left FIMT | 0.55(0.05) | 0.53(0.06) | 0.54(0.05)**@** | 0.123 |
| Mean FIMT | 0.54(0.05) | 0.52(0.06) | 0.53(0.05) | 0.221 |

**@**Right FIMT vs Left FIMT, p <0.001 (paired t-test).

**Table 4: Relationship Between Age and Femoral Intima Media Thickness**

|  |  |  |  |
| --- | --- | --- | --- |
| Variable |  |  | Post hoc (Games-Howell) test p-values |
| FIMTMean(SD)mm | p -value\* | Age group ≤ 40 years vrs 41 to 60 years | Age group ≤ 40 years vrs > 60 years | Age group 41 to 60 years vrs >60 years |
| Age group (years) ≤ 40 years 41 to 60 years > 60 years | 0.49(0.02)0.52(0.04)0.59(0.06) | <0.001 | 0.014 | <0.001 | 0.001 |

\*Welch test (F=20.534, df=25.8). vrs= versus.

**Figure 1: Scatter plot diagram showing relationship of FIMT (a) with Age and**

 **(b) with BMI.**

**(a)**



 Pearson Correlation Coefficient, r=0.719, p<0.001

**(b)**



 Pearson Correlation Coefficient, r=0.008, p=0.952