Normative Clinical Reference for Intima-media Thickness of Carotid Arteries among Nigerian Adults

Abstract
Background: The intima-media thickness (IMT) of the carotid arteries is said to be predictive of the risk of cerebrovascular accidents in patients and said to be affected by sex, age, and race. The lack of normative reference values of carotid IMT can adversely affect the screening of subclinical atherosclerosis in Nigeria. Sonography is the most widely used tool in clinical practice for IMT determination. Aim: This study was aimed at obtaining sonographic reference values of the IMT of the carotid arteries of healthy adult Nigerians for clinical use. Study Design: This is a prospective study, where participants were selected by a simple random technique. Setting: The study was carried out in 2019 on adult Nigerians from different ethnic backgrounds that resided in Bayelsa State. Materials and Methods: The study population was 104 healthy Nigerian adults both male and female between 18 and 64 years of age. Excluded were those without informed consent, Nigerians aged below 18 and above 65 years, anyone with a history of cardiovascular, cerebrovascular, or metabolic disorders, and athletes. After confirming normal blood pressure and taking their physical measurements, participants' necks were scanned with an "EcoMed" ultrasound machine version VERTU-3 Portable USG with a linear transducer and a frequency of 7.0 MHz by an experienced radiologist. Results: The IMT was recorded for the subjects in millimetres where common carotid artery: males = 0.487 ± 0.014, females = 0.480 ± 0.010 with a reference range of 0.200–0.750 mm; internal carotid artery: males = 0.500 ± 0.019, females = 0.459 ± 0.013 with a reference range of 0.200–0.750 mm; external carotid artery: males = 0.479 ± 0.018, females = 0.437 ± 0.014 with a reference range of 0.180–0.780 mm. The values for the males were higher than those of the females; however, they were not statistically significant. There was also no statistically significant difference between right and left sides in the IMT despite the right persistently being higher than the left in the general study population. Conclusion: This study has been able to provide reference values for IMT of the carotid arteries among Nigerians for clinical use in the meantime. We believe that a systematic review of similar data can further be done for the standardisation of national reference.

Keywords: Common carotid artery, external carotid artery, internal carotid artery, intima-media thickness, Nigerian adults, sexual dimorphism, sonography

Introduction
The intima-media thickness (IMT) of the carotid arteries is said to be predictive of the risk of cerebrovascular accidents in patients.[1-4] Arterial wall thickness affects vascular resistance and can influence the cerebral blood flow velocity and perfusion pressure,[5-7] and in the same vein, they can also be influenced by sex, the size of the body, the size of the neck, and some clinical parameters.[8] Because carotid IMT is said to provide an index of atherosclerotic vascular process that can be used to study subclinical atherosclerosis,[9] normative reference values in every society become invaluable data. In addition, ethnicity or race is said to further influence these values or their associations, which is important to ascertain[10,11] in every society. Sonography is the preferred investigative modality for the carotid IMT as it is easily accessible, affordable, and reliable in experienced hands.[12] Most clinicians now rely on it for diagnosis,[12] especially in our environment where other sophisticated modalities are not readily available or affordable by patients.

Presently, Nigeria lacks standardised data on healthy subjects. The lack of normative reference values of measurable carotid parameters makes the screening of subclinical atherosclerosis unrealistic and practically impossible.[13] Where these standard values are lacking (as in Nigeria), there is a need for studies to determine reference values for the different age groups, body sizes, and sex in our environment. This study was aimed to study subclinical atherosclerosis, normative reference values of measurable carotid parameters makes the screening of subclinical atherosclerosis unrealistic and practically impossible.
at obtaining sonographic values of the IMT of the carotid arteries of healthy adult Nigerians that could serve as a national standard for clinical reference in determining abnormality.

**Materials and Methods**

This is a prospective study. The study was carried out on Nigerians from different ethnic backgrounds that resided in Bayelsa State, Nigeria, in 2019. The study population was 104 healthy Nigerian adults both male and female between 18 and 64 years of age. Institutional ethical approval was obtained for the study. All subjects gave an informed consent and participated voluntarily. Participants were randomly selected without ethnic restriction. There was also no intention to skew the data to favour any ethnic Nigerian group as it was not part of the inclusion/exclusion criteria. Excluded from this study were those without informed consent, Nigerians aged below 18 and above 65 years, anyone with a history of cardiovascular, cerebrovascular, or metabolic disorders, athletes, and foreigners.

All subjects had their clinical vitals (pulse, blood pressure within normal range) and anthropometric values (weight, height, and neck and waist circumferences) taken before the sonographic study. The ultrasound machine used was a VERTU-3 Portable USG by “EcoMed” (Shenzhen, China) with a linear transducer and a frequency of 7.0 MHz that could be enhanced to 10MHz. An experienced radiologist scanned the subjects. The subjects were positioned supine and each carotid triangle exposed by tilting the head to the contralateral side. Doppler ultrasound scans of the common carotid artery (CCA), internal carotid artery (ICA), and external carotid artery (ECA) on both sides of the neck were done and measurements of their IMT taken 1 cm before the bulb of the CCA for CCA IMT measurement and 1 cm after bifurcation for either ICA or ECA in the end-diastole. \[14,15\] Two-dimensional measurements in B-mode and greyscale were made to obtain the values. Data were analysed using IBM SPSS v22 for t-test, and results were expressed as tables.

**Results**

The descriptive statistics of the IMT of the carotid arteries (CCA, ICA, as well as the ECA) is presented in Table 1. The mean age of subjects was 28.32 ± 9.09 years with 62 males and 42 females. The following mean values were recorded for male subjects in millimetres: CCA = 0.487 ± 0.014 [right (R) = 0.490 ± 0.014, left (L) = 0.484 ± 0.014 with a reference range of 0.200–0.800], ICA = 0.500 ± 0.014 (R = 0.497 ± 0.013, L = 0.503 ± 0.014) with a reference range of 0.200–0.800, ECA = 0.479 ± 0.018 (R = 0.487 ± 0.020, L = 0.471 ± 0.016) with a reference range of 0.150–0.850, whereas for females: CCA = 0.480 ± 0.010 (R = 0.481 ± 0.009, L = 0.479 ± 0.011) with a reference range of 0.300–0.700, ICA = 0.459 ± 0.013 (R = 0.474 ± 0.014, L = 0.445 ± 0.013) with a reference range of 0.200–0.700, ECA = 0.437 ± 0.014 (R = 0.448 ± 0.001, L = 0.426 ± 0.018) with a reference range of 0.200–0.700. The values for the males were higher than those of the females; however, they were not statistically significant. There was also no statistically significant difference between the right and left sides in the IMT despite the right persistently being higher than the left except for the ICA in the males; however, in the general study population, the right was still higher than the left in all three arteries. The reference range of values for the IMT of the carotid arteries was calculated using the formulae according to Kirkwood and Sterne, 2003, and Lawless and Fredette, 2005, which are represented in Table 2. The sonography of the carotid arteries is shown in Figure 1.

\[
\text{Range} = m \pm t_{0.975, n} \cdot \sqrt{\frac{n+1}{n}} \cdot S.D
\]

where \( t_{0.975, n} = 1.96 \), \( m = \text{mean} \), \( n = \text{sample size} \), and \( S.D = \text{standard deviation} \).

**Discussion**

There are numerous studies globally on the IMT of the carotid arteries in the literature. Even among Nigerians, there are several published works; however, they lack a normative range of values for clinical references for Nigerian subjects as these studies are mostly on hypertensive, diabetic, or unhealthy patients. This is the only study that provides a reference range among the few on normotensives that tend to bridge that research gap that would help Nigerian clinicians to diagnose an abnormal carotid thickness based on local data for clinical reference as the values vary globally because of race or ethnicity.\[^{10,11}\]

From our study, sexual dimorphism in the carotid IMT was not found as seen in other studies despite the males having

| Carotid artery | Male (62) | Female (42) | Total (104) |
|----------------|----------|-------------|-------------|
|                | Min      | Max | Mean | SD | Min | Max | Mean | SD | Min | Max | Mean | SD |
| Right CCA      | 0.200    | 0.900 | 0.490 | 0.0139 | 0.300 | 0.700 | 0.481 | 0.0089 | 0.200 | 0.900 | 0.487 | 0.0121 |
| Right ICA      | 0.200    | 0.900 | 0.497 | 0.0132 | 0.200 | 0.900 | 0.474 | 0.0136 | 0.200 | 0.900 | 0.488 | 0.0133 |
| Right ECA      | 0.200    | 1.700 | 0.487 | 0.0200 | 0.200 | 0.600 | 0.448 | 0.0099 | 0.200 | 1.700 | 0.471 | 0.0168 |
| Left CCA       | 0.200    | 1.200 | 0.484 | 0.0139 | 0.300 | 0.900 | 0.479 | 0.0112 | 0.200 | 1.200 | 0.482 | 0.0128 |
| Left ICA       | 0.200    | 0.900 | 0.503 | 0.0144 | 0.200 | 0.800 | 0.445 | 0.0129 | 0.200 | 0.900 | 0.480 | 0.0140 |
| Left ECA       | 0.100    | 0.800 | 0.471 | 0.0159 | 0.200 | 1.400 | 0.426 | 0.0180 | 0.100 | 1.400 | 0.453 | 0.0168 |

Max = maximum, Min = minimum, SD = standard deviation
higher values than the females. This has been demonstrated in similar studies in other climes.\textsuperscript{16} Umeh et al. from Nigeria had reported a significant sexual difference in IMT values,\textsuperscript{17} which we could not demonstrate in the index study. Apart from the above, we like to infer that the measurements of either right or left CCAs can be used for an individual in clinical practice as the differences in their thickness from our study was not statistically significant; more so, atherosclerosis (if it is the diagnosis of interest) is a systemic disease\textsuperscript{18} and would not be side-selective. Another Nigerian study has also shown this side-to-side statistically insignificant difference in normotensives.\textsuperscript{19} Interestingly, except for the IMT of the right ICA, which was noted to be slightly higher than that of the right CCA, wall thickness followed a pattern of CCA > ICA > ECA. In addition to this, findings from our study appeared to be peculiar in comparison with the two other studies from Nigeria that measured IMT of normotensive subjects with respect to our lower mean values, which is explainable as a majority of our study subjects were young and healthy between the ages 20 and 40 years with a mean age of 28.32 ± 9.09 years. Our study participants were similar despite the males having higher values. In Turkey, children aged 7–15 years with a mean IMT of 0.46 mm had no significant sexual difference, whereas sexual dimorphism has been reported in the same population.\textsuperscript{16} In Finland, healthy subjects with IMT had sexual difference that was attenuated when adjusted for risk factors and carotid diameter. Their men had 0.59 mm whereas the women had 0.57 mm.\textsuperscript{19} So, for men and women with similar risk factors and carotid diameter, sexual dimorphism was not demonstrable in their study. This is what was obtained in our study: both sexes had similar BMI, age group, and low risk for cardiovascular or cerebrovascular disease; hence their carotid wall thicknesses were similar despite the males having higher values. In contrast, the Sudanese study showed that the females had higher IMT values than the men, which was also not significant statistically. Furthermore, it was also noted that the BMI of the females was also higher than that of males in the latter study.\textsuperscript{21} In the United States, different study subgroups show differential increased wall thickening. Even though, IMT of carotid arteries among blacks was reported to be higher than whites in the United States\textsuperscript{23} it may not be solely because of race as we have seen from the results of our index study, where findings were even lower than some Caucasian values. Other factors relating to food, environment, and lifestyle need to be explored too; hence there is a need for society-based or group-based reference values.\textsuperscript{20}
Because carotid wall thickness assesses the risk of ischaemic stroke in adults, normative IMT values would serve as a reference and better guide clinical decision-making in terms of prevention and lifestyle modification at early stages of disease during screening among subclinical persons with abnormality.

Conclusion

We believe that results of our study could be used as a reference for assessing subclinical abnormality of the IMT of the carotid arteries, which are very useful in risk stratification in cerebrovascular disease in adults. Although the index study may be limited in sample size and stratification for all age groups, it is still useful data. We believe that systematic reviews may be necessary for further evaluation and finalisation of Nigerian data to fill the gap as a national standard.

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Conflicts of interest

There are no conflicts of interest.

References

1. Manterola HL, Lo Vercio L, Diaz A, Del Fresno M, Larrabide I. Validation of an open-source tool for measuring carotid lumen diameter and intima-media thickness. Ultrasound Med Biol 2018;44:1873-81.
2. Saba L, Banchoor SK, Arakic T, Viskovic K, Londehe ND, Lairde JR, et al. Intra- and inter-operator reproducibility of automated cloud-based carotid lumen diameter ultrasound measurement. Indian Heart J 2018;1394:19.
3. Rashid SA, Mahmud SA. Correlation between carotid artery intima-media thickness and luminal diameter with body mass index and other cardiovascular risk factors in adults. Sultan Qaboos Univ Med J 2015;15:c344-50.
4. Eigenbrodt ML, Sukhija R, Rose KM, Tracy RE, Couper DJ, Evans GW, et al. Common carotid artery wall thickness and external diameter as predictors of prevalent and incident cardiac events in a large population study. Cardiovasc Ultrasound 2007;5:11.
5. Yazici B, Ergoğlu B, Tugay A. Cerebral blood flow measurements of the extracranial carotid and vertebral arteries with Doppler ultrasonography in healthy adults. Diagn Interv Radiol 2005;11:195-8.
6. Guo XJ, Wu M, Pei SF, Xie P, Wu MY. Influence of carotid intima-media thickness levels at bifurcation on short-term functional outcomes among non-cardiogenic ischemic stroke patients with and without type 2 diabetes mellitus. Diabetes Metab Syndr Obes 2022;15:897-906.
7. Pomella N, Wilhelm EN, Kolyva C, González-Alonso J, Rakobowchuk M, Khir AW. Common carotid artery diameter, blood flow velocity and wave intensity responses at rest and during exercise in young healthy humans: A reproducibility study. Ultrasound Med Biol 2017;43:943-57.
8. Krejza J, Arkuszewski M, Kasner SE, Weigle J, Ustymowicz A, Hurst RW, et al. Carotid artery diameter in men and women and the relation to body and neck size. Stroke 2006;37:1103-5.
9. Järvisalo MJ, Putto-Laurila A, Jartti L, Lehtimäki T, Solakivi T, Rönnermäki T, et al. Carotid artery intima-media thickness in children with type 1 diabetes. Diabetes 2002;51:493-8.
10. Koskinen SM, Soine L, Valanne L, Silvennoinen H. The normal internal carotid artery: A computed tomography angiographic study. Neuroradiology 2014;56:723-9.
11. Ranadive SM, Yan H, Lane AD, Kappus RM, Cook MD, Sun P, et al. Aerobic exercise training and arterial changes in African Americans versus Caucasians. Med Sci Sports Exerc 2016;48:90-7.
12. Slovut DP, Romero JM, Hannon KM, Dick J, Jaff MR. Detection of common carotid artery stenosis using duplex ultrasonography: A validation study with computed tomographic angiography. J Vasc Surg 2010;51:65-70.
13. Juonala M, Kahonen M, Laitinen T, Hurri-Kahonen N, Eero J, Taittonen L, et al. Effect of age and sex on carotid intima-media thickness, elasticity and brachial endothelial function in healthy adults: The cardiovascular risk in Young Finns study. Eur Heart J 2008;29:1198-206.
14. Needleman L, Epelman MS, Grant EG, Paushter DM, Pellerito JS, Scott LM, et al. Ultrasound examination of the extracranial cerebrovascular system. J Ultrasound Med 2016;35.
15. Japanese Society of Ultrasound in Medicine. Standard method for ultrasound evaluation of carotid artery lesions. J Med Ultrason 2009;36:501-8.
16. Kocygır A, Doğan M, Yılmaz İ, Çağlar M, Hatipoğlu C. Relation of age and sex with carotid intima media thickness in healthy children. Turkish J Med Sci 2014;72:422-6.
17. Umeh EO, Agunloye AM, Adekanmi AJ, Adeginya AO. Ultrasound evaluation of intima-media thickness of carotid arteries in adults with primary hypertension at Ibadan, Nigeria. West Afr J Med 2013;32:62-7.
18. Lahoz C, Mostaza JM. Atherosclerosis as a systemic disease. Rev Española Cardiol Curr 2007;60:184-95.
19. Soneye MA, Adekanmi AJ, Obajimi MO, Aje A. Intima-media thickness of femoral arteries and carotids among an adult hypertensive Nigerian population: A case-control study to assess their use as surrogate markers of atherosclerosis. Ann Afr Med 2019;18:158-66.
20. Freitas PD, Piccinato CE, Martins WDP, Filho FM. Carotid atherosclerosis evaluated by Doppler ultrasound: Association with risk factors and systemic arterial disease. J Vasc Bras 2008;7:298-307.
21. Mahmoud MZ. Sonography of common carotid artery stenosis using duplex ultrasonography: A computed tomography angiographic study. Neuroradiology 2014;56:723-9.
22. Ranadive SM, Yan H, Lane AD, Kappus RM, Cook MD, Sun P, et al. Aerobic exercise training and arterial changes in African Americans versus Caucasians. Med Sci Sports Exerc 2016;48:90-7.
23. Ohira T, Shahar E, Iso H, Chambless LE, Rosamond WD, et al. Carotid artery wall thickness and incident cardiovascular events: The atherosclerosis risk in communities study. Stroke 2011;42:397-403.