Intima-Media Thickness of the Common Femoral Artery in a Black Kenyan Population: Correlation with Age, Gender and Geometric Factors

Julius A. Ogeng’o *, Musa K. Misiani, Nafula M. Ogeng’o, Philip M. Maseghe, Isaac K. Cheruiyot and Jecinta W. Waciuri

Abstract: Femoral artery intima-media thickness is a reliable surrogate marker of atherosclerosis and is important for prediction of coronary and peripheral vascular disease, but is seldom reported among black Sub Saharan African populations. This study, therefore, aimed at describing the intima-media thickness of the femoral artery in relation with age, gender and some of its geometric factors. Materials for this study were obtained during autopsy from 208 adult black Kenyans (154 males, 54 females, mean age 36.4 years) who had died of non cardiovascular causes. Those with history of cardiovascular risk factors were excluded. Femoral artery was exposed by dissection. Terminal branching pattern was recorded, and length and bifurcation angle measured. Materials for determination of intima-media thickness were processed routinely for paraffin embedding and sectioning. Five micron sections were stained with Mason’s trichrome, examined with light microscope and pictures taken. The images were digitized and intimal and medial thickness determined according to the protocol by Nakashima et al. [1]. The mean intima-media thickness was 0.76 ± 0.016 mm. It increased with age and was higher in males than females; for trifurcations (0.95 ± 0.032 mm) and also short arteries and those with wide bifurcation angles. Age and gender differences and those between arterial trifurcation and bifurcation attained statistical significance. In conclusion, the mean femoral intima-media thickness of the black Kenyan population studied is higher than those reported for Caucasian populations, increases with age and is higher in males and cases of trifurcation. This suggests that the study population is susceptible to atherosclerosis and that variant terminal branching pattern constitutes a geometric risk factor for atherosclerosis. We recommend ultrasound screening for those at risk.

Keywords: Intima-media thickness, Femoral, Geometric factors, African.

INTRODUCTION

Intima-media thickness of the femoral artery (f-IMT) is an established surrogate marker of atherosclerosis [2] and a reliable sensitive marker of subclinical atherosclerosis [3-5]. It is also emerging as a valuable independent predictor of extent and severity of coronary artery disease [6-8] and novel cardiovascular risk marker in generalized atherosclerosis [9]. It correlates with carotid intima-media thickness (c-IMT) [10] which shows ethnic variation. For example, black African Caribbeans have greater c-IMT than white Europeans and South Asians [11-15]. Femoral IMT, however, does not explicitly show significant ethnic differences [12, 16-19]; although age adjusted f - IMT gender differences manifest in whites only [18]. Further, f-IMT is a surrogate predictor of peripheral artery disease (PAD) [12,17,20]. The prevalence of PAD is higher among black Americans than in Non Hispanic Whites (NHW), Hispanics and South Asians [21-23] and is higher in Sub Saharan African (SSA) countries than in developed predominantly Caucasian and Indo-Asian ones [24-27]. Studies of f-IMT, however, among black SSA populations are few. As PAD emerges to be a major problem in SSA including Kenya [28], the importance of surrogate markers gains prominence to inform early intervention. This study therefore aimed at determining intima-media thickness of the common femoral artery in relation to age, gender and its geometric factors in a black Kenyan population.

MATERIALS AND METHODS

Materials for this study were obtained during autopsy from femoral arteries of 208 adult black Kenyans (154 males, 54 females; mean age 36.4; range 19-75 years) who had died of trauma. The causes of death included road traffic accident (121; 58.2%); gunshot (53; 25.5%); burns (19; 9.1%); fall from a height (8; 3.8%) and electrocution (7; 3.4%). Information on past medical and lifestyle history was provided by the next of kin. Those with history of hypertension, smoking, diabetes mellitus, coronary heart disease, peripheral vascular disease (PVD), stroke and those whose body mass index was >29 kgm⁻² were excluded.

The individuals were divided into four age groups as shown in Table 1.
Table 1: Age and Gender Distribution of the Study Population

<table>
<thead>
<tr>
<th>Age group</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-30</td>
<td>31</td>
<td>5</td>
<td>36</td>
</tr>
<tr>
<td>31-50</td>
<td>69</td>
<td>35</td>
<td>104</td>
</tr>
<tr>
<td>51-70</td>
<td>45</td>
<td>11</td>
<td>56</td>
</tr>
<tr>
<td>71-90</td>
<td>9</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>154</td>
<td>54</td>
<td>208</td>
</tr>
</tbody>
</table>

The femoral arteries (104 left; 104 right) were exposed by dissection. The common femoral artery (CFA) was defined as that arterial segment extending between the inguinal ligament and femoral bifurcation (FB). The length of the CFA was measured between inguinal ligament and FB in millimeters. The angle between superficial femoral artery (SFA) and profunda femoris artery (PFA) was measured only in cases of bifurcation. Specimens for morphometry were taken from the middle of each artery within 72 hours of death, to avoid overt postmortem damage to the tissues. Two-millimeter-long specimens were fixed by immersion in 10% formaldehyde solution and processed routinely for paraffin embedding. Five micrometer sections were stained with Mason’s trichrome for demonstration of mural components.

Morphometry was done on digitized light microscopy slides in which the entire wall thickness could be visualised. Ten slides from each artery were chosen by systematic random sampling in which every fourth slide was picked. Analogue photographs were taken using a photo microscope at a constant magnification of X35. The photographs were then scanned using a hp scanner and analyzed using Scion Image™ Multiscan software. Intimal and medial thickness was measured based on the protocol by Nakashima et al. [1], in which the extent of the intima was defined as between the lumen and the internal elastic lamina. Four random points (ISa, ISb, ISC, ISd) were selected and the average size computed. The media was defined as the area between the internal elastic lamina and the external elastic lamina. Four random points (Msa, Msb, Msc, Msd) were selected and the average size computed (Figure 1).

Data were tested for normality and analysed using SPSS version 21.0, Chicago, Illinois. Student t-test was used to analyse the differences between side, gender, age, branching patterns, bifurcation angle and length at 95% confidence interval in which P-value of ≤ 0.05 was taken as statistically significant. The results are presented in a macrograph, bar graph and tables.

Figure 1: Measurement of intimal and medial Size: IS = intimal size; MS = medial size.

RESULTS

The mean f-IMT was 0.76 ± 0.016 mm (range: 0.45-1.05mm). In majority of the cases (158; 76%) it was due to tunica media which comprised 70-90% (Figure 2A, B). In 50 (24%) cases there was severe intimal hyperplasia with the tunica intima comprising 70 - 85% of the IMT. Such intimal thickenings were predominantly fibrocellular (Figure 2C, D).

Correlation of f-IMT with Age and Gender

f - IMT was higher in males (0.815 ± 0.012 mm); than in females (0.712 ± 0.015 mm). The difference was statistically significant (p = 0.023). It progressively increased with age such that it was 0.69 ± 0.014 mm in those under 30 years and 0.94 ± 0.03 mm in those over 70 years (Figure 3). The difference between those aged below 50 years and those above 50 years was statistically significant (p = 0.0312).

Correlation of f-IMT with Geometric Factors

The CFA bifurcated in 71.2% and trifurcated into SFA, PFA and lateral circumflex femoral artery in 28.8% of cases. In cases of bifurcation, the mean f-IMT was 0.72 ± 0.014 mm (range 0.43-1.08 mm) while in trifurcation it was 0.95 ± 0.032 mm (range 0.75-1.25 mm). The difference was statistically significant (p = 0.006).
Figure 3: Variation of f-IMT with age among black Kenyans.

The f-IMT increased with bifurcation angle from 0.75 mm in those ranging ≤ 20°; to 0.85 mm in those >30° (Table 3). The difference, however, did not attain statistical significance (p = 0.0605).

Table 3: Variation of f-IMT with Bifurcation Angle of CFA in a Black Kenyan Population

<table>
<thead>
<tr>
<th>Angle range</th>
<th>f-IMT (mm) Mean± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-20</td>
<td>0.75±0.014</td>
</tr>
<tr>
<td>21-25</td>
<td>0.78±0.016</td>
</tr>
<tr>
<td>26-30</td>
<td>0.84±0.023</td>
</tr>
<tr>
<td>&gt;30°</td>
<td>0.85±0.013</td>
</tr>
</tbody>
</table>

Figure 2A-D: Distribution of relative Intima - media thickening in common femoral artery in a black Kenyan Population. TI = Tunica Intima; TM = Tunica Media; TA = Tunica Adventitia. Mason’s trichrome stain. X 100. A: Whole wall thickness in a 47-year-old male. Note the predominance of tunica media occupying over 80% of the IMT. B: Whole wall thickness in a 55-year-old female showing predominance of TM, with substantial thickening of TI. C: Whole wall thickness in a 65-year-old male. Note the marked of thickening of TI and its high cellularity. D: Whole wall thickness in a 73-year-old male showing marked thickness of the tunica intima to occupy over 80% of IMT. Note the fibrocellular nature of subendothelial zone (sez).
The f-IMT decreased with length of CFA. For those measuring ≤ 5cm the mean f-IMT was 0.72 ± 0.013 mm while for those measuring >10 cm, it was 0.65 ± 0.015 mm (Table 4). The difference was not statistically significant (p = 0.0721).

Table 4: Variations of f-IMT with Length of CFA in a Black Kenyan Population

<table>
<thead>
<tr>
<th>Length</th>
<th>Male (f-IMT ± SE)</th>
<th>Female (f-IMT ± SE)</th>
<th>Overall (f-IMT ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>-</td>
<td>0.65 ± 0.011</td>
<td>0.74 ± 0.012</td>
</tr>
<tr>
<td>11-20</td>
<td>0.72 ± 0.012</td>
<td>0.61 ± 0.008</td>
<td>0.69 ± 0.010</td>
</tr>
<tr>
<td>21-30</td>
<td>0.67 ± 0.012</td>
<td>0.60 ± 0.01</td>
<td>0.65 ± 0.015</td>
</tr>
<tr>
<td>31-40</td>
<td>0.67 ± 0.016</td>
<td>0.60 ± 0.013</td>
<td>0.65 ± 0.013</td>
</tr>
<tr>
<td>41-50</td>
<td>0.66 ± 0.015</td>
<td>0.59 ± 0.011</td>
<td>0.65 ± 0.012</td>
</tr>
<tr>
<td>51-60</td>
<td>0.64 ± 0.016</td>
<td>0.58 ± 0.013</td>
<td>0.64 ± 0.010</td>
</tr>
<tr>
<td>&gt;60</td>
<td>0.64 ± 0.017</td>
<td>0.57 ± 0.016</td>
<td>0.63 ± 0.012</td>
</tr>
</tbody>
</table>

DISCUSSION

The mean f-IMT of 0.76 mm is higher than contemporary literature reports from Caucasian populations, which reveal 0.52-0.719 mm [29,30]. Notably, it is substantially higher than the reference level of 0.562 mm reported in the French population [31] (Table 5).

Table 5: Common Femoral Artery IMT in Various Populations

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>N</th>
<th>Method</th>
<th>f-IMT (mm) Overall Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>[31]</td>
<td>French</td>
<td>98</td>
<td>Ultrasound</td>
<td>0.562 ± 0.74</td>
</tr>
<tr>
<td>[32]</td>
<td>Belgian</td>
<td>156</td>
<td>Ultrasound</td>
<td>0.52 ± 0.62</td>
</tr>
<tr>
<td>[29]</td>
<td>Caucasian</td>
<td>188</td>
<td>Ultrasound</td>
<td>0.719 ± 0.8</td>
</tr>
<tr>
<td>[33]</td>
<td>American</td>
<td>160</td>
<td>Ultrasound</td>
<td>0.49 ± 0.22</td>
</tr>
<tr>
<td>[12]</td>
<td>UK</td>
<td>98</td>
<td>Ultrasound</td>
<td>0.571 ± 0.061</td>
</tr>
<tr>
<td>[30]</td>
<td>Dutch</td>
<td>256</td>
<td>Ultrasound</td>
<td>0.52 ± 0.06</td>
</tr>
<tr>
<td>[18]</td>
<td>White Black</td>
<td>210</td>
<td>Ultrasound</td>
<td>0.71 ± 0.05</td>
</tr>
<tr>
<td>Current study</td>
<td>Kenyan</td>
<td>208</td>
<td>Micrometry</td>
<td>0.76 ± 0.016</td>
</tr>
</tbody>
</table>

Although the method of study was different from those in the other studies, values of IMT measured by ultrasound have been shown to correlate with those from histology and in many cases to be higher [34-37]. Accordingly, the higher values recorded in the current study suggest population variations, probably related to genetic and epigenetic factors, which manifest in arterial geometry.

Femoral artery IMT has recently gained prominence as a cardiovascular risk marker which correlates with the number of risk factors [9,17,33], and a surrogate indicator of coronary and peripheral vascular disease [12,17]. The higher value observed in the current study suggests that both coronary artery and peripheral artery disease are prominent in this population. Indeed recent studies indicate that myocardial infarction is the most common cause of cardiovascular death in the population [38] and peripheral vascular disease is not uncommon [28].

In nearly 25% of cases, there was severe intimal hyperplasia, a feature that heralds atherosclerosis and correlates with its risk factors [39-41]. This implies that a substantial number of asymptomatic individuals may suffer pre clinical femoral artery atherosclerosis. PERTINENT to this suggestion is the report that non atheromatous intimal thickening is a consistent feature of PVD [42]. The high prevalence of intimal hyperplasia is consistent with the prevalence of PVD among the black African populations [24,25,27]. Proactive measures should be taken against this condition.

Correlation with Age and Gender

The f-IMT increased with age and was higher in males than in females. This is consistent with reports of higher prevalence of PVD in advancing age [12,17,22,31,33]. It suggests that atherosclerosis of the femoral artery is more common in older individuals, and in males than in females irrespective of risk factor profile. Indeed, PVD in SSA occurs more commonly in males than in females and increases with age [28,43]. Accordingly, even in the absence of known modifiable risk factors older men with suggestive features should be screened for atherosclerotic cardiovascular disease.

Correlation with Geometric Factors

A remarkable finding of the current study is that the f-IMT was high despite exclusion of individuals with cardiovascular risk factors. This suggests that there are non-modifiable risk factors which influence f-IMT. PERTINENT to this suggestion is the observation that f-IMT was higher for trifurcation, short arteries and those with higher angles of bifurcation. The only variable, however, in which the difference in f-IMT was statistically significant was terminal branching pattern. This implies that only this feature may significantly influence atherogenesis in this artery. The higher f-IMT in variant branching pattern is consistent with recent
findings in the common carotid arteries in which carotid IMT increased with the number of terminal branches [44]. The high IMT is probably due to disturbed flow, reduced wall shear stress experienced at such variant branching sites [45,46], which predisposes to atherosclerosis. Accordingly, over 28% of the population in whom the CFA trifurcated may be more prone to atherosclerosis of CFA and SFA. This is consistent with the pattern of lesion distribution of PAD observed in the Kenyan population [28]. Individuals with unusual branching patterns should therefore be screened for PVD.

CONCLUSION

The mean f-IMT of the Kenyan population is higher than those reported previously, and is also higher in males, in older individuals and in cases of CFA trifurcation. This suggests that the study population is susceptible to atherosclerosis and that variant terminal branching pattern is a geometric risk factor for atherogenesis. The high prevalence of severe intimal hyperplasia implies that atherosclerotic PVD is a common problem in the population. We recommend Ultrasound screening for those who are vulnerable, and proactive preventive measures against atherosclerosis.

AKNOWLEDGEMENT

We are grateful to Martin Inyimili, Judith Machira, Margaret Irungu and Acleus Murunga for technical assistance and Antonina Odock-Opiko for typing the manuscript.

CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES


Received on 07-12-2015   Accepted on 20-03-2016   Published on 10-05-2016

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