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Research article

ANATOMICAL RISK FACTORS FOR ATHEROSCLEROSIS OF LEFT COMMON CAROTID ARTERY IN A BLACK KENYAN POPULATION

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Running Title: Anatomical risk factors for atherosclerosis

SUMMARY

Carotid birfucation anatomy influences predisposistion to atherosclerosis, which is a common cause of ischaemic stroke. Due to increased prevalence of stroke in Sub-Saharan Africa, this study undertook to establish whether or not the population has geometric risk factors for atherosclerosis. Common carotid arteries were exposed by dissection in 208 cadavers and autopsy specimens of adult black Kenyans. The arteries were cleared of fibrofatty tissue and internal jugular vein and nerves retracted away. Mandible was also removed, branches exposed and followed to their destinations. Pattern of termination of common carotid artery was recorded and representative photographs taken with a high resolution digital camera. Angles of bifurcation were measured. Internal diameters of common, internal and external carotid arteries were measured and outlet: inlet area ratios calculated. Intimomedial thickness was determined and correlated with pattern of termination, bifurcation area ratio and angle. Frequencies, means and standard deviations were determined using SPPS17.0 for windows.

The commonest mode of termination was bifurcation (58.9%) followed by trifurcation (26.8%), quadrififcation (5.4%) and pentafurcation (1.7%). Mean bifurcation outlet: inlet ratio was 1.05, with 35.7% being above 12 and 30.4% being below 1.0. The mean angle of bifurcation was 24.1° (Range 9° to 39°). Most of the cases were between 20° and 30°. Among the cases studied, 30.4% were below 20° while 19.6% were above 30°. Intimomedial thickness increased with number of branches, bifurcation angle and area ratio.

Over 25% of the carotid bifurcations in the study population have anatomical risk factors for atherosclerosis, namely additional branches, wide bifurcation angle and non-optimal area ratio. Control measures against atherosclerosis should start early.

Keywords: anatomical risk, population, atherosclerosis, stroke

INTRODUCTION

Carotid artery atherosclerosis is the commonest cause of ischaemic stroke (Syo *et al.*, 2005; Mazighi *et al.*, 2008). The carotid bifurcation is the most commonly involved site (Fisher and Fiemann, 1990; Schulz and Rothwell, 2003). Prevalence of carotid bifurcation lesions shows individual, gender and ethnic variations (Schulz and Rothwell, 2000; Syo *et al.,* 2005). These ethnic differences persist after adjusting the various externally modifiable risk factors (Inzitari *et al.* 1990; Khan *et al.,* 2011). This suggests that such variations are attributable to genetic predisposition manifesting in morphological characteristics of the involved arteries (Kim *et al.*, 2005).

The variations are attributable to genetically influenced carotid birfucation anatomy and geometry (Thomas *et al.*, 2005; Koch *et al.,* 2009). As stroke becomes a major problem in Sub-Saharan Africa including Kenya (Mensah 2008; Jowi and Mativo *et al.,* 2008), it is important to determine whether or not these geometric risk factors exist. The geometric risk factors known to predispose to atherosclerosis are bifurcation angle; luminal ratio of outlet to inlet vessels; branching pattern (Schulz and Rothwell, 2000; Thomas *et al.,* 2005; Phan *et al.,* 2012). Data on these factors are important in influencing early identification of patients at risk of atherosclerosis for aggressive intervention (Phan *et al.,* 2012). They are also important in intervention procedures such as diagnostic interventional radiology, stenting or endarterctomy (Ozgur *et al.,* 2008; Natris *et al.,* 2011). The current study therefore examined the carotid bifurcation for the anatomical risk factors of atherosclerosis.

MATERIALS AND METHODS

Materials for this study were cadavers and autopsy specimens at Department of Human Anatomy, University of Nairobi, Kenya.

Skin and fascia were removed from the left side of the neck to expose sternocleidomastoid muscle which was detached from both attachments. The body of the mandible was also removed to allow full access to the carotid bifurcation. The carotid sheath was opened and fibrofatty tissue and internal jugular vein removed. Nerves were retracted, carotid bifurcation exposed, internal and external carotid arteries identified.

Number of branches proximal to and at the bifurcation were counted and each identified by tracing it to its destination. In cases of bifurcation, the internal angle between the branches was measured to the nearest ½ of a degree using a pair of dividers. Sections were taken from the common, internal and external carotid arteries 5mm away from the bifurcation, processed for paraffin wax embedding and sectioning. 7µm sections stained with Hematoxylin and Eosin stains were examined using Scion Image analyzer. The radius and area were determined and ratio of outlet to inlet calculated as ICA + ECA: CCA. Intimomedial thickness was measured on these microscopic sections using the protocol developed by Nakashima et al., (2002).

RESULTS

Five patterns of branching were identified. Bifurcation was the most common (58.6%). Of the remainder (41.4%), the most common pattern was trifurcation (26.9%). Quadrifurcation and pentafurcation of the CCA were observed in 5.3% and 1.4% of the cases respectively. The superior thyroid artery (STA) branched from the CCA in 4 (7.7%) of the cases.

The mean angle of bifurcation was 24.1° (Range 9° to 39°). Most of the cases were between 20° and 30°. Among the cases studied, 30.4% were below 20° while 19.6% were above 30°. Mean bifurcation outlet: inlet ratio was 1.05, (range 0.6 – 2.0). 35.7% were above 1.2 and 30.4% being below 1.0. The majority (58.2%) were between 1.1 – 2.0 mm. Mean carotid intimomedial thickness was 0.86 ± 0.05mm. Males had a thicker intimal medial thickness (0.97± 0.02) when compared to females (0.77±0.06), [p = 0.05]. The carotid intimal medial thickness increased with age; 0.5 ± 0.016mm, 0.87 ± 0.014mm and 1.21 ± 0.06 mm for the age groups 0 – 20, 21 – 40, and

>40 respectively [p = 0.035]. Mean IMT also increased with the number of branches from 0.89 ± 0.022mm for bifurcation to 1.27 ± 0.024mm for pentafurcation. The differences were stastically significant (Table 1). Mean IMT also increased with bifurcation angle (Table 2). The mean for those with angles $<20^0$ was 0.65 ± 0.06; while that for angle $>20^0$ was 0.92 ± 0.17. The difference was statistically significant. [p = 0.039]

Table 1: Mean c-IMT of respective branching patterns of CCA among black Kenyans.

Branching Pattern	**IMT**		**Pvalue**
	Mean ± SE	**Range**	
Bifurcation	Overall 0.89 ± 0.022	0.46 – 1.18	0.046
	Male 0.97 ± 0.022	0.52 – 1.48	
	Female 0.74 ± 0.066	0.46 – 1.39	
Trifurcation	Overall 0.98 ± 0.031	0.52 – 1.56	0.039
	Male 0.99 ± 0.015	0.53 – 1.56	
	Female 0.88 ± 0.024	0.52 – 1.48	
Quadrifurcation	Overall 1.06 ± 0.042	0.72 – 1.76	0.04
	Male 1.08 ± 0.017	0.74 – 1.76	
	Female 0.99 ± 0.031	0.72 – 1.68	
Pentafurcation	Overall 1.27 ± 0.052	0.92 – 1.92	0.043
	Male 1.35 ± 0.024	0.95 – 1.92	
	Female 1.12 ± 0.012	0.92 – 1.86	

Table 2: Mean c-IMT of CCA correlated with bifurcation angle in a black Kenyan population.

Range	**IMT (Mean + SE)**
6 – 10	0.52 ± 0.016
11 – 15	0.63 ± 0.028
16 – 20	0.71 ± 0.032
21 – 25	0.83 ± 0.021
26 – 30	0.92 ± 0.016
>30	1.02 ± 0.012

The c – IMT decreased with increasing bifurcation area ratio that is the higher the ratio the lower the c – IMT. For example the mean c – IMT was 0.87 ± 0.02mm for bifurcation area ratio 2.1 – 2.5; and 1.33 ± 0.04mm for ratio range 0 – 0.5. (Table 13)

Table 13: Mean c – IMT compared with bifurcation area ratio of Left CCA in a black Kenyan population.

Range of bifurcation area ratio	c – IMT (Mean ± SE) mm
0 – 0.5	1.33 ± 0.03
0.6 – 1.0	1.29 ± 0.06
1.1 – 1.5	0.92 ± 0.02
1.6 – 2.0	0.89 ± 0.03
2.1 – 2.5	0.87 ± 0.02

The ratio of 1.2 was taken as the cut – off point. In this case, the mean c – IMT for those with ratio less than 1.2 was 0.30 ± 0.04mm, while that for those greater than 1.2 was 0.90 ± 0.01mm. The difference was statistically significant [p = 0.025].

DISCUSSION

Branching Pattern

The common carotid artery usually divides into external and internal carotid arteries (Standring, 2008). Observations of the current study revealed, however, that this bifurcation only occurs in 58.9% of cases, 41.1% of the arteries being variant. The most frequent variation was trifurcation in 26.9%. Explicit accounts of common carotid trifurcation are only in the form of case reports (Gurbuz et al., 2001; Chitra, 2008; Jadhar et al., 2011).

Quadrifurcation and pentafurcation occurred in 5.3% and 1.4% respectively. Literature is silent on these variations, with only one isolated case report of pentafurcation into a common linguo-facial trunk, occipital, ascending pharyngeal, external and internal carotid arteries (Kishve et al., 2011). Presence of a third or higher order branch alters hemodynamics that results in associated endothelial injury implicated in atherogenesis (Fischer and Fieman, 1990; Ross, 1990; Fuster et al., 1992). Alteration of the branching angle can also increase the risk of atherosclerosis (Moore et al., 2010; Furuichi et al., 2007). Indeed observations of the current study revealed that increasing number of branches were positively associated with high c – IMT. This implies that individuals found to show variant carotid termination should be followed up for atherosclerosis.

Bifurcation angle

The mean bifurcation angle was 24.1°, within the range of 15 – 48.5^0 reported in literature (Table 35). This figure, while comparable to 20^0 reported in an American population (Kamenskiy et al., 2012) is lower than 40^0 reported in the Croatian one (De Syo et al., 2005). This implies ethnic variability in bifurcation angle probably depending on age (Mitomiya and Karino, 1984; Thomas et al., 2005). This might provide part of the explanation for ethnic differences in predilection to atherosclerosis.

Table 35: Bifurcation angle of the common carotid artery in different populations

Reference	Population	Method	Bifurcation angle (°)
Thomas *et al*., 2005 [387]	Canadian	MRI	Young- 48.5 Old- 63.6
Kamenskiy *et al*., 2012 [625]	American	CTA	15
Mark *et al*., 2010 [628]	German	CTA	20
Fisher and Fieman, 1990 [263]	American	Angiography	34.0
De Syo et al.., 2005 [626]	Croatian	Angiography	40.5

Current study, 2013	**Kenyan**	**Dissection**	**24.1**

Indeed observations of the current study reveal a high proportion of CB with wide angles. Since wide angles are associated with atherosclerosis risk (Moore et al., 2010; Sun and Cao, 2011), these findings imply higher vulnerability to atherosclerosis in this population. Pertinent to this suggestion is the observation in the present study that wider angles of bifurcation were significantly associated with higher c – IMT.

Bifurcation area ratios

Observations of the current study reveal a mean bifurcation area ratio of 1.06 (Range: 0.62 - 1.60). This is larger than 0.83 reported for an English population (Schultz and Rothwell, 2001) but lower than those reported for most other studies (Table 36).

Table 36: Bifurcation area ratios of the common carotid artery in different populations

Reference	Population	Mean bifurcation area ratio
Spelde *et al*., 1990 [629]	Dutch	1.47
Williams & Nicolaides [630]	English	1.19
Schulz and Rothwell [265]	English	0.83
Beare *et al*., 2011 [631]	Australian	1.28
Thomas *et al*., 2005 [387]	Canadian	1.19(old); 1.32 (young)
Mark *et al*., 2010 [628]	German	1.8
Sehirli *et al*., 2005 [632]	Turkish	1.14
Mitomiya and Karino, 1984 [627]	Japanese	1.19
Current study, 2013	**Kenyan**	**1.06**

In 35.7% of the cases it was higher than 1.2, the ratio considered to be the most significant geometric risk factor for atherosclerosis (Goubergrits et al., 2001). On the other hand, 30.4 % were less than 0.99 reported for diseased vessels (Spelde et al., 1990). Postmortem studies have revealed a close reationship between IMT or plaque formation and reduced outflow/inflow ratio suggesting that a greater outflow area reduces shear stress in daughter vessels, promoting local atherosclerosis (Fischer and Fieman, 1990; Mitomiya and Karino, 1984; Spelde et al., 1990). This implies that 35.7% of the CBs in the Kenyan population are prone to atheroclerosis on the basis of outflow ratio. Pertinent to this suggestion is the observation that higher ratios were associated with higher c – IMT. These figures suggest ethnic variability in bifurcation area ratios which may constitute part of the explanation for variability in susceptibility to atherosclerosis. Since the variability of these ratios increase with age or early atherosclerosis (Thomas et al., 2005), they will depend on mean age of population.

CONCLUSION

Over 25% of the carotid bifurcations in this black African population have anatomical risk factors for atherosclerosis, namely additional branches, wide bifurcation angles and non – optimal bifurcation area ratio. Control measures against atherosclerosis should start early.

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