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Original Article

Distribution of carotid artery intima-media thickness among ischaemic stroke patients and its association with common risk factors - a cross-sectional study

Dinithi Chithrani Ginneliya

Postgraduate Institute of Medicine, University of Colombo, Sri Lanka.

Key words: **carotid artery intima-media thickness, Ischaemic stroke, Atherosclerosis**

Abstract

Background

Increased carotid intima-media thickness (CIMT) has been frequently observed with ischaemic stroke but the relationship between CIMT and common risk factors in ischaemic stroke patients in our community was not evaluated.

Objective

This study aims to describe the distribution of CIMT among ischaemic stroke patients and determine its association with common risk factors.

Methods

The study was conducted as a descriptive cross-sectional study in which 204 ischaemic stroke patients were followed up at Teaching Hospital, Karapitiya, from July to December 2023. CIMT measurements of both carotid arteries were obtained using B-mode ultrasound. Risk factor data were collected through an interviewer-administered questionnaire. CIMT values above 0.80 mm were classified as abnormal. Statistical analysis was carried out using SPSS 21.0, with a significant level of 0.05.

Results

The sample's mean age was 60.74 years (SD = 12.51). Mean CIMT for the right carotid artery was 0.87 mm (SD = 0.64), and for the left, 0.88 mm (SD = 0.50), with no significant difference between the two sides ($P > 0.05$). Among patients, 58.0% and 52.1% had abnormal right and left CIMT, respectively. Significant differences in CIMT were found between males and females ($P < 0.05$). No significant associations were observed between CIMT and hypertension or diabetes mellitus ($P > 0.05$). Risk of abnormal CIMT was higher in dyslipidaemic patients (OR 3.46;95% CI: 1.89–6.34, $P < 0.0001$). A one-way ANOVA test revealed a significant difference in CIMT between smokers and ex-smokers with non-smokers ($P = 0.03$). Hierarchical logistic regression indicated that all combined factors accounted for 39.4% of the variability in abnormal CIMT, although none emerged as significant independent risk factors.

Conclusions

Abnormal CIMT was significantly associated with dyslipidemia and smoking among ischaemic stroke patients. However, further studies with comparative groups are needed to fully determine the association between CIMT and ischemic stroke risk.

Corresponding Author: Dinithi Chithrani Ginneliya, E-mail< dinithiginneliya@gmail.com >
https://orcid.org/0009-0003-3700-8778

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Introduction

Stroke stands behind ischaemic heart disease as the second leading cause of death worldwide. On average, one person dies of a stroke every four minutes somewhere in the world [1]. It also causes a major health and economic burden to developing countries. Ischaemic strokes have several etiological factors, both modifiable and non-modifiable [2]. Age and gender are non-modifiable risk factors. Modifiable risk factors include hypertension, dyslipidaemia, diabetes mellitus, and smoking. Atherosclerosis, being the common underlying pathophysiology, comes hand in hand with all these risk factors. It causes an increase in the thickness of vascular intima and media, resulting in the narrowing of the lumen.

Since stroke is a devastating condition, primary prevention is an essential healthcare concern, and therefore, the early identification of individuals at risk is crucial. Many studies have been done to assess the prevalence of ischemic stroke in relation to the presence of modifiable risk factors, including hypertension, diabetes, dyslipidaemia, and smoking. These studies [3,4] have confirmed a strong correlation between the incidence of stroke and the above factors.

A revised Framingham stroke risk score was done in 2019, which is aimed at the introduction of a scoring system using nontraditional risk markers in the prediction of stroke [2]. More recent studies have aimed at the identification of non-conventional risk markers to assess the incidence of stroke. These include coronary artery calcium (CAC), carotid artery intima-media thickness (CIMT), ankle-brachial index (ABI), and high-sensitivity CRP. Among these markers, CIMT has shown a significant relationship with the incidence of stroke [2].

An increase in (CIMT) is one of the earliest changes in the arterial wall in the process of atherosclerosis. Carotid artery intima-media thickness (CIMT), which is measured using a Doppler scan, gives an estimation of the overall assessment of atherosclerotic thickening of the vascular wall and is a surrogate marker of atherosclerosis and, therefore, a risk marker of ischemic stroke. It is a parameter that can be measured easily using Doppler ultrasound, which is a non-invasive, safe method.

A cross-sectional study done in the Neurosonology Division of the University of Indonesia has shown that the correlation between CIMT and stroke is statistically significant [5].
Another study done in India, assessing the age-wise association of CIMT on ischaemic stroke, has proven there is a strong correlation of CIMT with the incidence of stroke, even in young age groups, implying it may be used as a predictor of cerebrovascular events in all age groups in the Indian population [6]. Further, the variation of CIMT with the age and sex of normal individuals has been studied [7]. It is also found that the significant difference in CIMT between patients with acute ischemic stroke and controls persists across all age groups [8].

A study done on carotid artery intima-media thickness and hypertensive heart disease by Costan G. Magnuseen [9] has shown that CIMT is elevated in hypertensive patients. The study titled “Effects of Cigarette Smoking on carotid artery atherosclerosis: a community-

based cohort study" done by Hiroyuki Kiriyama, Hidehiro Kaneko, Yuriko Yoshida, Koki Nakanshi and Yoshiko Mizuno [10] has shown that exposure to smoking and duration of smoking are significant risk factors for carotid atherosclerosis.

A cross-sectional study done in China [4] to identify factors associated with increased CIMT in low-income Chinese populations has shown a lower mean CIMT in their population compared to the values in non-Asian populations. This study also revealed a negative association between mean CIMT and some of the risk factors of stroke, including hypertension and dyslipidaemia.

Most of the studies done show an association of CIMT with individual risk factors for stroke. Hardly any data is available in studies that have assessed multiple risk factors at the same time in a single population, allowing comparison of the association of each modifiable risk factor with CIMT. There can be geographic and racial differences in CIMT. The degree of its association with the risk factors of stroke may depend on lifestyle and medical management of the associated comorbidities. There is a very limited number of published Sri Lankan studies in this area of research.

Therefore, it is important to conduct the proposed study in our population. This study would be a preliminary for a more detailed study on the use of CIMT as a predictor of ischemic stroke in day-to-day practice, allowing clinicians early identification of patients at risk of developing stroke.

Methods

The study was carried out as a descriptive cross-sectional study from July 2022 to January 2023 at the Department of Radiology, Teaching Hospital Karapitiya, Sri Lanka, which is a tertiary care center. Permission to conduct the study was obtained from the Director of T H Karapitiya. Consent was taken from the relevant consultants referring the patients for the Carotid Doppler study. Ethics clearance was obtained by the ethics review committee of the National Hospital of Sri Lanka. Data was stored securely in a password-protected database at the Department of Radiology, T H Karapitiya. Data was analyzed using SPSS (Statistical Package of Social Sciences)

The study population were patients referred to the Department of Radiology, TH Karapitiya for a carotid artery Doppler scan following a recent event of ischaemic stroke. Only patients after the first episode of ischaemic stroke were selected. The stroke should have been confirmed clinically or by a CT scan of the brain. Patients with haemorrhagic strokes, multiple repeated strokes, and unconscious patients were excluded. The study was carried out over 6 months, recruiting all the eligible patients presenting within that period. Patient data were collected using an interviewer-administered questionnaire. The details of comorbid factors (hypertension, diabetes and dyslipidaemia) were obtained from patient records and cross-checked with information gathered from the patient and clinical records. A smoking history was taken from the patient and they were categorised into smokers, non-smokers, and ex-smokers. Ex-smokers were defined as those who had completely stopped smoking for at least three months.

Participants underwent B-mode ultrasonography of both the right and left carotid arteries. All IMT Measurements were done using the TOSHIBA Aplio 500 ultrasound scanner available at the Doppler scan unit at the Department of Radiology, T.H. Karapitiya. Measurement of carotid IMT was done by the principal investigator according to the standardized protocol [11], which is summarized below.

High-resolution B mode system, linear probe with a frequency of 7.5 MHz. Frame rate is selected as >15-25 Hz, and frame depth is kept at 30mm to 40mm. Gain settings were adjusted optimally to facilitate edge detection and zoom not used.

The common carotid artery wall was assessed longitudinally and perpendicular to the ultrasound beam with minimal compression. The horizontal position of the artery was maintained in the image sector to optimize the visualization of the lumen-intima interface. CIMT was measured at 1cm proximal to bifurcation using a semi-automatic IMT measurement tool. Three values were taken for each common carotid artery (right & left), and the three values were averaged.

The normal levels of CIMT have been defined in different studies in the literature with slight variations in the level. However, this variation is mostly attributed to variation in different ethnic groups, which could be attributed to the lifestyle and medical management of co-morbidities.

In our study, CIMT values were grouped as follows, according to a study done by Fromm et al. [12]. CIMT was defined as normal when <0.8mm, as suspected of arterial disease when 0.8-0.99 mm and as pathological when 1.0 mm or more. Plaques were defined as CIMT more than 1.5mm. CIMT above 0.8 was considered abnormal.

Results

A total of 204 patients who presented for a carotid artery Doppler following a first episode of ischemic stroke were analyzed in the study. The mean age of the sample was 60.74 (SD=12.52) years. The age distribution comprised over 60 years (57.80%), 40 to 60 years (32.4%) and 20 to 40 years (9.8%). Most (63.2%, n=129) were male.

Co-morbidities in the study sample included hypertension 136 (66.7%), diabetes mellitus 74 (36.3%) and dyslipidemia 100 (49%).

Sixty-five percent of patients were non-smokers, 19.2% were current smokers, and 15.8% were ex-smokers. Table 1 depicts the descriptive statistics of smoking details collected only from the current smokers. The mean duration of smoking among current smokers was 25.62 years (SD= ± 9.09), while the minimum duration is 10 years, and the maximum duration is 42 years. The mean number of cigarettes used per day was 7.56 (SD=± 3.96), ranging from 2 to 15 per day.

Table 1: Descriptive statistics of Smoking details

	Smoking details	
	Duration of Smoking (Years)	Number of cigarettes per day
Mean ± SD	25.62 ± 9.09	7.56 ± 3.96
Minimum	10	2
Maximum	42	15
Mode	30	8

The mean intimal medial thickness of the right carotid artery was 0.87 mm (SD=±0.64), ranging from 0.56 mm to 9.85 mm. The mean value for the left carotid artery was 0.88 mm (SD= ± 0.50), ranging from 0.59 mm to 6.97mm. There was no significant difference between the two sides (P > 0.05). (Table 2)

Table 1: Intimal Medial Thickness Measurements (in mm)

	Minimum	Maximum	Mean ± SD
Right	0.56	9.85	0.87 ±0.64
Left	0.59	6.97	0.88 ± 0.50

Most patients over 60 years of age (61%, n=72) had right CIMT suspected of arterial disease. Most male patients (72.2%, n=93) had abnormal right CIMT (suspected of arterial disease, pathological or plaques). Most female patients (58.7%, n=44) had normal right CIMT (Table 3).

Table 3: Association between Right CIMT and Demographic Factors

Factors	**Right CIMT**			
	Normal	**Abnormal**		
	<0.8 (N=80)	0.8-0.99(N=103)	>1.0(N=20)	>1.5(N=1)
Age				
20-40 Years	15(75.0)	2(10.0)	3(15.0)	0(0.0)
40-60 Years	32(48.5)	29(43.9)	5(7.6)	0(0.0)
>60 Years	33(28.0)	72(61.0)	12(10.2)	1(0.8)
Gender				
Male	36(27.9)	74(57.4)	18(14.0)	1(0.8)
Female	44(58.7)	29(38.7)	2(2.7)	0(0.0)

Seventy-seven patients (65.3%) above 60 years had left CIMT above 0.8 mm. Out of the 129 male patients, the left CIMT was abnormal in 81(62.9%). The majority (60%, n=45) of the female patients had normal left CIMT, while none of them had plaques. Considering all patients, 58.0% had abnormal right CIMT, and 52.1% had abnormal left CIMT, respectively. Considering both right and left measurements, a significant difference in CIMT was found between males and females ($P < 0.05$) (Table 4).

Table 4: Association between left CIMT with demographic factors

	Left CIMT			
	Normal	**Abnormal**		
	<0.8(N=93)	0.8-0.99(N=81)	>1.0(N=28)	>1.5(N=2)
Age				
20-40 Years	15(75.0)	3(15.0)	2(10.0)	0(0.0)
40-60 Years	37(56.1)	22(33.3)	7(10.6)	0(0.0)
>60 Years	41(34.7)	56(47.5)	19(16.1)	2(1.7)
Gender				
Male	48(37.2)	53(41.1)	26(20.2)	2(1.6)
Female	45(60.0)	28(37.3)	2(2.7)	0(0.0)

Among 100 patients with dyslipidaemia, the majority (76%, n=76) had right CIMT above 0.8 mm. (Table 5).

Table 5: Association between right CIMT with comorbidities

Comorbidities	**Right CIMT**			
	Normal	Abnormal		
	<0.8(N=80)	0.8-0.99(N=103)	>1.0(N=20)	>1.5(N=1)
HTN	48(35.3)	76(55.9)	11(8.1)	1(0.7)
DM	26(35.1)	46(44.7)	2(10.0)	0(0.0)
DL	24(24.0)	65(65.0)	10(10.0)	1(1.0)

Regarding patients with dyslipidemia, 67(67%) had CIMT above 0.8 mm. No significant associations were observed between CIMT and hypertension or diabetes mellitus ($P > 0.05$). However, the risk of abnormal CIMT was higher in dyslipidaemic patients (OR 3.46;95% CI: 1.89–6.34, $P < 0.0001$) (Table 6).

Table 6: Association between left CIMT with comorbidities.

Comorbidities	Left CIMT			
	Normal	Abnormal		
	<0.8(N=93)	0.8-0.99(N=81)	>1.0(N=28)	>1.5(N=2)
HTN	59(43.4)	58(42.6)	17(12.5)	2(1.5)
DM	29(39.2)	34(45.9)	10(13.5)	1(1.4)
DL	33(33.0)	49(49.0)	16(16.0)	2(2.0)

Neither non-smokers nor ex-smokers had plaques in the right carotid arteries. Current smokers' mean smoking duration was significantly associated with the right CIMT (p=0.033). The right CIMT increased with an increase in the mean duration of smoking. (Table 7).

Table 7: Association between right CIMT with smoking details

	Right CIMT				P Value
	<0.8(N=80)	0.8-0.99 (N=103)	>1.0 (N=20)	>1.5 (N=1)	
Non-smoker	67(50.8)	63(47.7)	2(1.5)	0(0.0)	-
Smoker	5(12.8)	24(61.5)	9(23.1)	1(2.6)	-
Ex-smoker	8(25.0)	15(46.9)	9(28.1)	0(0.0)	-
Duration of smoking (Mean ± SD)	15.83±5.26	25.97±7.99	28.69±10.19	-	**0.033**
Number of cigarettes per day (Mean ± SD)	6.83±4.35	6.79±4.09	9.06±3.41	-	0.150

Similarly, the mean duration of smoking was significantly associated with the left CIMT (p=0.010). The left CIMT shows a progressive incline with the mean duration of smoking.

A one-way ANOVA test revealed a significant difference in CIMT between smokers and ex-smokers with non-smokers (P = 0.03). (Table 8)

Table 8: Association between left CIMT and smoking

	Left CIMT				P Value
	<0.8(N=93)	0.8-0.99(N=81)	>1.0(N=28)	>1.5(N=2)	
Non-smoker	74(56.1)	55(41.7)	3(2.3)	0(0.0)	-
Smoker	5(12.8)	17(43.6)	16(41.0)	1(2.6)	
Ex-smoker	14(43.8)	8(25.0)	9(28.1)	1(3.1)	
Duration of smoking (Mean ± SD)	16.50±4.87	27.76±9.11	26.14±8.58	34±2.82	**0.010**
Number of cigarettes per day (Mean ± SD)	6.13±4.58	6.76±3.49	9.10±4.01	5.50±0.70	0.143

Hierarchical logistic regression indicated that all combined factors accounted for 39.4% of the variability in abnormal CIMT, although none emerged as significant independent risk factors.

Discussion

In this study, the mean age was 60.74 and the majority (63.2%) were male patients. Hypertension was the most common co-morbidity detected, while dyslipidemia was present in approximately half of the population. The majority were non-smokers (65%). The mean duration of smoking among current smokers was 25.62 years (SD= ± 9.09), while the minimum duration was 10 years, and the maximum duration was 42 years. The mean number of cigarettes used per day was 7.56 (SD=± 3.96), ranging from 2 to 15 per day. The mean IMT of the right carotid artery was 0.87 mm (SD=±0.64), ranging from 0.56 mm to 9.85 mm. The mean value for the left carotid artery was 0.88 mm (SD= ± 0.50), ranging from 0.59 mm to 6.97mm. Considering all patients, 58.0% and 52.1% had abnormal right and left CIMT, respectively. Males had higher CIMT values compared to females, both on the right and left. There was a significant difference in CIMT between males and females ($P < 0.05$). The majority (75%, n=15) of 20 to 40 years had both normal right and left CIMT. Of patients between 40 and 60, approximately half had normal CIMT, 48.5% (n=32) on the right and 56.1%(n=37) on the left. Most of the patients over 60 years of age had CIMT above 0.8 mm, 85 (72.2%) on the right and 77 (65.3%) on the left.

The study showed no significant association between CIMT and hypertension or CIMT and diabetes mellitus ($P > 0.05$). However, the risk of abnormal CIMT was higher in dyslipidemic patients ($P < 0.0001$). The mean duration of smoking was statistically significantly associated with both right and left CIMT.

Limited studies are available in the literature on the evaluation of CIMT on the right and left sides. Rodriguez Hernandez et al. elicited that hypertensive subjects had higher

values of CIMT on the left side [13]. In our study, the mean CIMT of the right and left sides were approximately the same, and no significant difference was found between the two sides ($P > 0.05$).

Multiple studies have assessed the risk factors for increased CIMT and the presence of carotid plaques. Similar to our study, these studies have explored the association between traditional cardiovascular or cerebrovascular risk factors, such as serum lipid parameters, age, gender, hypertension, diabetes, and smoking [3,4]. In our study, age more than 60 years, male gender, dyslipidemia and being a current smoker have increased the right and left CIMT.

Fromm A. et al. have revealed that increased internal carotid artery IMT was associated with dyslipidemia and stroke and increased carotid artery bifurcation IMT was associated with dyslipidemia, coronary heart disease, and smoking [12]. A study in China [14] analyzed 793 patients with hyperlipidemia, not on statins, who developed non-cardioembolic ischemic stroke and elicited a conclusion supporting the above fact. Age, smoking, hypertension, HDL cholesterol, and diabetes mellitus were associated with mean IMT, and the same risk factors bar hypertension, were associated with maximum CIMT. The baseline mean CIMT of this study, 0.89mm, was similar to ours.

A case-control study including 163 diagnosed cases of first-time ischemic stroke and age and gender-matched healthy control attendants at a tertiary care hospital revealed that the age-specific CIMT was significantly higher in stroke cases than in age-matched controls across all age groups [6]. Even though our study did not include a control group, both the right and left CIMT showed an increasing size pattern when moving from the 20-40 category to more than 60 age categories.

The same study that right CIMT, along with a history of hypertension, is an important risk factor for ischemic stroke in the younger age group (20-40 years). Our study failed to elicit a similar result concerning hypertension or diabetes mellitus, but an abnormal CIMT was significantly associated with dyslipidemia and smoking. We revealed a significant difference in CIMT between smokers and ex-smokers with non-smokers. Also, the mean duration of smoking was statistically significantly associated with abnormal CIMT.

Since this study included only patients who had ischemic strokes but no controls, further studies with comparative groups are needed to fully determine the association between CIMT and ischemic stroke risk. Another limitation of our study is that we consider a single cut-off value for CIMT for all ages. Since there is a normal variation of CIMT, which gradually increases with age, a future study may use appropriate normal values for different age groups.

The findings of this study are an impetus for further studies in this area, especially to identify the importance of measurement of CIMT in patients with atherosclerosis as a screening tool to assess the risk of future stroke.

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