Relevance of Carotid Intima-Media Thickness and Plaque Morphology in the Risk Assessment of Patients with Acute Ischemic Cerebral Infarcts: A Case-Control Study of Large Series from a Single Center

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Abstract

Background: Carotid atherosclerosis is not only a marker of systemic atherosclerosis but also a predictor of ischemic stroke. The purpose of this study is to correlate the relationship between atherosclerotic risk factors, plaque categories, percentage of stenosis, stroke subtypes, and carotid intima-media thickness (CIMT) in patients with acute ischemic stroke. **Methods:** This case–control study was conducted over 4 years from December 2014 to December 2018. A total of 500 cases diagnosed with acute cerebral infarct using computed tomography or magnetic resonance imaging were included in the study. Two hundred and fifty healthy controls were studied for the presence of atherosclerotic risk factors and carotid artery IMT by B-mode Doppler ultrasonography. The IMT value thus calculated was 0.79 mm and such a value would include >95% of the controls. Carotid plaques were detected from both sides of IMT measurement of the carotid system. **Results:** A total of 500 cases of acute infarct and 250 healthy controls were included in this case–control study. CIMT was abnormal in 348 cases with 192 males and 156 females with a mean value of 0.912 ± 0.124 against 0.794 ± 0.132; $P < 0.001$ controls. Mean CIMT (averaged right and left) varied directly according to the increasing plaque stenosis ranging from 0.70 mm to 0.96 mm in males and 0.68 mm to 0.94 mm in females ranging from no plaque to cases with ≥50% stenosis ($P < 0.001$ across stenosis categories). On multivariate analysis, CIMT (>0.79) remained associated as compared to other variables (PR [Probability] 5.33, 95% confidence interval: 1.398–22.784; $P = 0.012$). Mean right CIMT of patients with lacunar infarction, cardioembolism, and large artery stroke was 0.886 ± 0.230, 0.919 ± 0.171, and 0.938 ± 0.169 mm, respectively ($P = 0.032$). Mean left CIMT of patients with lacunar infarction, cardioembolism, and large artery stroke was 0.884 ± 0.195, 0.916 ± 0.144, and 0.930 ± 0.137 mm, respectively ($P = 0.034$). **Conclusion:** CIMT measurements are independent markers of acute ischemic cerebral infarcts. In the current study, CIMT was found to be higher among acute ischemic stroke patients who were the elderly, smoker, hypertensive, diabetic, and hypercholesterolemic than that of nonsmoker, normotensive, nondiabetic, and normocholesterolemic controls.

Keywords: Acute ischemic cerebral infarct, carotid intima-media thickness, common carotid artery, plaque category, stenosis, stroke subtypes

Introduction

Carotid atherosclerosis is not only a marker of systemic atherosclerosis but also a predictor of ischemic stroke.[1] Measurement of carotid intima-media thickness (CIMT) on B-mode Doppler ultrasonography is completely noninvasive, does not involve radiation, cost-effective and has psychological advantages of an imaging tool for assessment of the severity of atherosclerosis, as patients and physicians tend to believe invisible structures rather than abstract concepts. The incidence of stroke increases with increasing age and with the growing elderly population worldwide, the number of patients with stroke are likely to increase.[2] In most of the ischemic strokes,

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the underlying pathophysiology is atherosclerosis. The risk factors for stroke are modifiable and nonmodifiable. The modifiable risk factors are mostly related to the atherosclerotic burden and include diabetes, hypertension (HTN), smoking, and hyperlipidemia.[3] Several risk prediction scoring systems have been evolved to identify individuals with high risk. However, most of these scoring systems have some limitations.[4] TOAST classification of ischemic stroke subtypes includes:[5]

1. Large-artery atherosclerosis (embolus/thrombosis): these patients will have clinical and brain imaging findings of either significant (>50%) stenosis or occlusion of a major brain artery or branch cortical artery, presumably due to atherosclerosis
2. Cardioembolism (high-risk/medium-risk): this category includes patients with arterial occlusions presumably due to an embolus arising in the heart
3. Small-vessel occlusion (lacunae): this category includes patients whose strokes are often labeled as lacunar infarcts
4. Stroke of other determined etiology: this category includes patients with rare causes of stroke such as nonatherosclerotic vasculopathies, hypercoagulable states, or hematologic disorders
5. Stroke of undetermined etiology: the cause of a stroke cannot be determined with any degree of confidence.

The CIMT has emerged as a reliable, independent marker of cardiovascular disease.[6] The purpose of this study is to correlate the relationship between atherosclerotic risk factors, stroke subtypes, and CIMT in patients with acute ischemic stroke.

Materials and Methods

This case–control study was conducted at the Department of Radiology, St. John's Medical College, Bengaluru, India, over 4 years from December 2014 to December 2018 with approval from the Institutional Ethical Committee. A total of 500 cases diagnosed with acute cerebral infarct using computed tomography or magnetic resonance imaging were included in the study. Two hundred and fifty healthy controls were studied for the presence of atherosclerotic risk factors and CIMT using B-mode Doppler ultrasonography. Controls were participants without stroke matched to cases by age, gender, and with no risk factors such as diabetes, HTN, smoking, and hypercholesterolemia. They were deemed healthy individuals without any evidence of clinical/silent stroke. Patients with carotid body tumors and acute cerebral venous thrombosis were excluded from the study.

Defining risk factors

The criteria for the presence of risk factors are as follows: (1) HTN – if measured blood pressure was ≥140/90 mmHg on two occasions and/or treated for HTN before stroke; (2) diabetes mellitus (DM) – if presented with a history of DM and/or were on diet control, hypoglycemic drugs or received insulin treatment or had ≥126 mg/dL fasting glucose and maintained the ≥200 mg/dL during hospital stay; (3) Smoking – "Smoker" group comprises ever smoker, current smoker, and ex-smoker. An "ever smoker" was defined as a person who self-reported smoking at least 100 cigarettes during the course of his/her lifetime or having smoked pipes or cigars for 6 months or more. A "current smoker" was defined as a person who self-reported smoking within the calendar year before the year of diagnosis, whereas an "ex-smoker" was defined as an ever smoker who had quit smoking for >1 calendar year before the diagnosis year. Nonsmoker group was defined as a person who did not meet the criteria for ever smoker, current smoker, or ex-smoker; and (4) hypercholesterolemia – considered when a patient who had a diagnosis of it and/or was on prescribed diet or lipid-lowering agents or had fasting cholesterol >200 mg/dl.

Defining carotid intima-media thickness cutoff

In the absence of a well-defined population cutoff value for CIMT, we used control mean IMT plus two standard deviations (SDs). The IMT value, thus calculated was 0.79 mm. Such a value would include >95% of the controls. Of the 500 cases, 348 cases had an IMT >0.79 mm, whereas 152 cases had a CIMT below this cutoff value. The same CIMT value was considered in both younger and older age groups. As expected, only one subject among the controls had IMT above this value. The sensitivity of this value was 48.33%, whereas the specificity was 96%. The positive predictive value was 93.55%, whereas the negative predictive value was 60.76%.

Defining plaque morphology

A plaque was defined as focal thickening of 50% greater than the surrounding area or greater than 1.5 mm. Each carotid was scanned for the category of plaques classified as minimal build up, calcified plaque, soft plaque, mixed calcified and soft plaques, and ulcerated plaques. Plaque composition was reported based on observed echogenicity as follows: (1) none: early buildup "calcified," where there was a thick calcified cap over the lesion; [Figure 1a] (2) soft: where there was little or no calcification of the plaque; [Figure 1b] and (3) mixed: where there was a combination of calcified and soft plaques [Figure 1c]. The soft plaque had lower level echoes appearing more echolucent. The calcified plaque had a more echo-dense appearance from sound waves that are more intensely reflected.

Data collection

Patients diagnosed with acute cerebral infarct by cross-sectional imaging were referred for carotid Doppler examination. The patient was placed in the supine position with a soft pillow behind the shoulders to provide adequate support, and the neck was slightly hyperextended for Doppler examination of the carotids. The CIMT measurements were made using Doppler with a 7.5 MHz linear superficial probe in B-mode placed on bilateral common carotid arteries in cases of acute cerebral infarct with slight compression to obtain good longitudinal image of the artery. CIMT measurement after obtaining a suitable image with adequate magnification, CIMT was measured on the far wall of the transducer with the first echoic line bordering the vessels lumen representing the lumen-intima interface; the second echogenic line is caused by the media-adventitia interface. The distance between these two lines represents the IMT of the carotid. Two plus-shaped calipers were used and hence that the first caliper is placed on the thick echogenic line in the carotid wall and the other cursor over the thin echogenic line toward the luminal anechoic area. Maximum distance between the two calipers was measured and recorded for each patient visually. The CIMT measurement of both right and left sides of the common carotid arteries was taken 1 cm proximal to the carotid bifurcation avoiding the plaque area, and the mean value was used for analysis. CIMT was determined by an average of two-point measurements made on either side irrespective of the side of the infarct. All readings were taken and interpreted by the same experienced technician. The ultrasound machine used had a sensitivity range of 0.1 mm, that is, each division was equivalent to 0.1 mm. Carotid plaque stenosis was selected for analysis on the side of the infarct.

Statistical analysis

Descriptive statistics was reported using numbers and percentages for categorical variables. Analysis was performed using the Microsoft Excel 2013 Microsoft Corp., Redmond, WA, USA, and SPSS Statistical Package (version 20.0), IBM SPSS Statistics for Windows, V.20.0, IBM Corp., Armonk, New York, USA. The Student's *t*-test for continuous variables and Chi-square test for categorical variables were used for statistical comparison. *P* values were calculated for comparison of age and sex among case and control groups, plaque categories, percentage of stenosis, and stroke subtypes. Participants were divided into control and stenosis groups, and the ANOVA test was performed. Multivariate analysis was performed on variables such as HTN, DM, hypercholesterolemia, current smoking, and age.

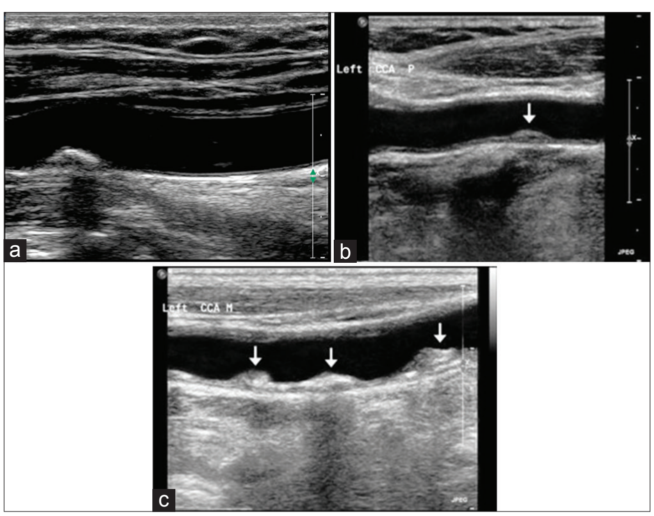

Figure 1: Defining plaque morphology. (a) Focal plaque at the far wall of the carotid bulb with calcification and acoustic shadowing. (b) Focal smooth homogenous plaque (arrow) located on the far wall of the proximal common carotid artery. (c) Moderate-to-large amount of heterogeneous multiple plaques (arrows) with focal calcification and irregular surface, in mid common carotid artery

Results

In the current study, CIMT values were significantly higher in patients with acute ischemic stroke when compared to controls, and this difference persisted across all age groups. The mean IMT in this study was 0.79 mm, which is similar to the values reported in other South-east Asian studies. In the current study, cases were in the age groups of 30–40, 40–50, 51–60, 61–70, and 71–80 years, and the mean age was 55.8 years in males and 55.2 years in females with maximum number of cases in the age group of 61–70 years (180 cases). Mean age in the cases group was 56.4 years and in the control group was 55.2 years. Mean age was 55.8 years for males and 56.2 years for females with a total of 280 and 220 cases, respectively. Mean age was 55.4 years for males and 56.0 years for females with a total of 165 and 85 controls, respectively. The lowest age was 34 years in males and 36 years in females with the highest age being 76 years and 78 years for male and female, respectively, in both groups. On comparing, gender distribution between case and control groups showed no significant difference [Table 1]. With increase in age among cases, mean CIMT has increased drastically compared to controls and showed a statistically significant difference (*P* = 0.041) [Table 1]. Mean CIMT in cases of 41–50 years is 0.8 mm, 51–60 years is 1.1 mm, and 61–70 years is 1.3 mm. In cases, mean CIMT value was 0.91, and in controls, mean CIMT was 0.79 mm. Mean CIMT is high in cases and controls with plaques when compared to cases and controls without plaques. Mean CIMT measurements in cases with risk factors were significantly higher when compared to controls with risk factors and comorbidities.

A total of 500 cases of acute infarct and 250 healthy controls were included in this case–control study. Among the 500 cases of ischemic stroke and 250 controls, mean CIMT values showed

Table 1: Comparison of age and sex among case and control groups

Age	Total number	Mean age (years)±SD	SEM	*P*
Cases	500	56.4±7.921	0.36	0.041*
Controls	250	55.2±7.646	0.48	
Sex	**Category**	**Total number of patients (%)**		***P***
Male	Case	280/500 (56)		0.655**
	Control	165/250 (66)		
Female	Case	220/500 (44)		
	Control	85/250 (34)		
	n	**Mean CIMT (mm)±SD**	**SEM**	***P***
Cases	500	0.912±0.124	0.005	<0.001
Controls	250	0.794±0.132	0.008	

*Independent *t*-test, **Chi-square test. SEM: Standard error of the mean, SD: Standard deviation, CIMT: Carotid intima-media thickness significant differences [Table 1]. Linear regression analysis was used to see if these differences were affected by age. Using these cross-sectional data and a linear regression model, the mean increase in CIMT with age was 0.2–0.3 mm/decade. The risk factors for stroke affecting CIMT were analyzed, and it showed that the CIMT correlated positively with age, smoking, HTN, DM, and hypercholesterolemia. The ischemic stroke patients with the presence of risk factors such as smoking, HTN, DM, and hypercholesterolemia presented with significantly higher CIMT values than patient with the absence of risk factors. CIMT was abnormal in 348 cases with 192 males and 156 females having IMT above 0.79 mm, whereas 152 cases had a CIMT below this cutoff value. The presence of plaques and % stenosis were quantified in both the carotids. Similar findings were looked for among the controls. Mean CIMT (averaged right and left) varied directly according to increasing plaque stenosis ranging from 0.70 mm to 0.96 mm in males and 0.68 mm to 0.94 mm in females ranging from no plaque to cases with ≥50% stenosis ($P < 0.001$ across stenosis categories) [Table 2]. Among 750 participants, there were 250 (33.3%) controls without any past ischemic event, 138 (18.4%) patients with <30% stenosis categorized as "Ischemic Group-I," 182 (24.3%) patients with 30%–50% stenosis categorized as "Ischemic Group-II," and 180 (24.0%) patients with >50% stenosis categorized as "Ischemic Group-III." Compared to the control group, patients from both Ischemic Group-II and Ischemic Group-III were significantly more often hypertensive and diabetic and had higher mean CIMT [Table 2]. The proportion of patients was least in Ischemic Group-I [Table 2]. Mean (SD) CIMT according to % stenosis, plaque category correlated with significant *P* values on performing one-way ANOVA test across groups such as controls ($P = 0.021$) and stenosis categories Ischemic Group-I ($P = 0.023$), Ischemic Group-II ($P = 0.019$), and Ischemic Group-III ($P = 0.022$) [Table 2]. Multivariate analysis was performed on variables that could potentially be a confounding factor and included variables of HTN, DM, hypercholesterolemia, current smoking, and age in the current study. CIMT (>0.79) remained associated as compared to other variables (PR 5.33, 95% confidence interval: 1.398–22.784; $P = 0.012$) [Table 3]. Plaque morphology, CIMT, stroke subtypes, and the most common % Stenosis category were correlated in the current study, and findings revealed ulcerated plaques to have maximum CIMT value of 0.89 mm followed by soft plaques with a CIMT value of 0.88 mm and mixed calcified and soft plaques with a value of 0.86 mm. Large artery stroke > lacunar infarct > cardioembolism is the order of incidence in calcified plaques, mixed calcified-soft plaques, ulcerated plaques, and soft plaques. However, lacunar infarcts were the majority in minimal buildup plaques. Cardioembolism was the most common stroke subtype in ulcerated plaques (14.3%). Soft plaques, mixed calcified-soft plaques, and ulcerated plaques had > 50% stenosis, whereas calcified plaques presented with 30%–50% stenosis and minimal buildup plaques had < 30% stenosis [Table 4]. The incidence of ischemic stroke subtypes such as large artery stroke, lacunar infarcts, and cardioembolic stroke showed a significant correlation with abnormal CIMT values and large artery stroke was the most common ($P < 0.001$). Mean right CIMT of patients with lacunar infarction, cardioembolism, and large artery stroke was 0.886 ± 0.230, 0.919 ± 0.171, and 0.938 ± 0.169 mm, respectively ($P = 0.032$). Mean left CIMT of patients with lacunar infarction, cardioembolism, and large artery stroke was 0.884 ± 0.195, 0.916 ± 0.144, and 0.930 ± 0.137 mm, respectively ($P = 0.034$).

Discussion

High-resolution ultrasonography of carotid artery provides a noninvasive assessment of atherosclerosis burden and cerebrovascular disease. Increased CIMT and complex plaque characteristics of carotid arteries are well-known risk factors for the same and the presence of arterial plaques represents an advanced stage of atherosclerosis and is regarded as a more powerful predictor of cardiovascular events than CIMT.[7] CIMT is a surrogate marker for the early detection of atheromatous changes and is easily accessed by noninvasive B-mode ultrasound. Consideration of both right and left carotids could improve the prediction by assuring the true presence of large parameters.[8] In this study, the presence of ischemic stroke was correlated with age, gender, CIMT of both the carotids, plaque categories, percentage of stenosis, and major stroke subtypes.

In the current study, both the carotids were measured for the IMT and were found to be significantly higher in cases (0.912 ± 0.124) than in controls (0.794 ± 0.132; $P < 0.001$), which persisted in different age groups. Cupini *et al*.[9] in their study reported a mean value of CIMT (>1 mm),

Table 2: Mean (standard deviation) carotid intima-media thickness according to stenosis, plaque category with results of one-way ANOVA test among groups

Category	Number of cases/total (%)	Mean CIMT (mm)	SEM	One-way ANOVA test	
				F	*P*
Controls	250/750 (33.3)	0.794	0.005	4.938	0.021
Ischemic group-I with <30% stenosis	138/750 (18.4)	0.830	0.012	5.231	0.023
Ischemic group-II with 30%-50% stenosis	182/750 (24.3)	0.910	0.008	6.813	0.019
Ischemic group-III with >50% stenosis	180/750 (24.0)	0.950	0.010	4.986	0.022
Ischemic groups with stenosis	500/750 (66.6)	0.896	0.010	7.211	0.017

SEM: Standard error of the mean, CIMT: Carotid intima-media thickness which was associated with the development of stroke as compared to 0.91 mm in controls; however, the study population was of >70 years of age and of different ethnicity. Mukherjee *et al*.[10] reported significantly higher CIMT values among stroke cases as compared to controls, but the mean values were lower (0.66 vs. 0.32 mm) than our study; however, the sample size was small, and the controls were not matched with the cases. GINIC,[11] a case–control study, had similar mean IMT values (0.79 mm) in stroke patients compared to our study. The basal characteristics of the population were similar to our study, except the study was done on a higher age group and only on hypertensive patients. Difference between stroke cases and controls was also observed by Sahoo *et al*.,[12] who reported significantly higher mean CIMT (0.782 ± 0.19 mm) than in controls (0.594 ± 0.98 mm; $P < 0.0001$) in the South Indian population. Similar to our study, the difference persisted across all age groups. Higher values of CIMT in stroke patients with DM, HTN, and smokers have been previously reported in the Caucasian population.

The current study also reported a higher value of CIMT among stroke cases with comorbidities, and the difference was statistically significant. Similar results were observed by Sahoo *et al*.,[12] where the difference was significant in the subgroup analysis by risk factors such as HTN, diabetes, and smoking between patients and controls. Similar to this study, the CIMT was significantly higher in hypertensive patients and smokers. Study in Eastern Indian tertiary care hospital by Saha *et al*.[13] in 50–60 years of age group also found a higher value of CIMT among ischemic stroke patients with diabetes in both left and right carotids as compared to controls, but the difference was not significant.

Table 3: Multivariate analysis of several variables and probability correlation

Variable	PR	95% CI	*P*
CIMT (>0.79 mm)	5.33	1.398-22.784	0.012
HTN	4.87	0.894-22.031	0.022
DM	2.34	0.361-12.452	0.037
Hypercholesterolemia	4.93	0.961-22.371	0.020
Current smoking	4.28	0.827-21.592	0.027
Age	4.51	0.941-20.127	0.025

HTN: Hypertension, DM: Diabetes mellitus, CI: Confidence interval, CIMT: Carotid intima-media thickness, PR: Probability

Rotterdam elderly case–control single-center study[14] in a subgroup of the population of 55 years of age or older also showed an association between common CIMT and the risk of stroke. A cross-sectional study by Salim Hasim in Southeast Asia also shows a strong association of CIMT (>1.0 mm) and stroke ($P = 0.008$) in the Indonesian population.[15] A direct correlation exists because IMT is a marker of generalized atherosclerosis, which plays an important role in the pathogenesis of cerebrovascular events such as stroke.

Conclusion

CIMT measurements are independent markers of acute ischemic cerebral infarcts. In the current study, CIMT was found to be higher among acute ischemic stroke patients who were elderly, smoker, hypertensive, diabetic, and hypercholesterolemic than nonsmoker, normotensive, nondiabetic, and normocholesterolemic controls.

Limitations of the study

Although adequate sample size was attained, it was a single-center study performed at a tertiary care hospital and was not a prospective study. Hence, the progression of IMT could not be studied.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Table 4: Correlation between plaque morphology, carotid intima-media thickness, stroke subtypes, and percentage stenosis category

Plaque category	Number of cases/total (%)	Cases, mm (SD)	Major stroke subtype (%)	Commonest % stenosis category	OR (95% CI)	*P*
No plaque	278/750 (37)	0.70 (0.11)	-	-	-	-
Minimal buildup	240/750 (32)	0.76 (0.11)	Lacunar infarction (8.8)	<30	2.61 (1.44-3.82)	0.044
Calcified plaque	65/750 (8.6)	0.82 (0.12)	Large artery stroke (12.4) > lacunar infarct (2.5) > cardioembolism (0.5)	30-50	2.73 (1.51-4.08)	0.035
Mixed calcified and soft plaque	55/750 (7.3)	0.86 (0.13)	Large artery stroke (16.6) > lacunar infarct (6.1) > cardioembolism (0.6)	>50	2.91 (1.63-4.27)	0.027
Ulcerated plaque	44/750 (5.8)	0.89 (0.14)	Large artery stroke (7.3) > lacunar infarct (2.2) > cardioembolism (14.3)	>50	3.09 (1.74-4.42)	0.023
Soft plaque	68/750 (9.0)	0.88 (0.14)	Large artery stroke (19.1) > lacunar infarct (8.4) > cardioembolism (1.2)	>50	2.97 (1.72-4.33)	0.031

SD: Standard deviation, OR: Odds ratio, CI: Confidence interval

References

1. Heiss G, Sharrett AR, Barnes R, Chambless LE, Szklo M, Alzola C. Carotid atherosclerosis measured by B-mode ultrasound in populations: Associations with cardiovascular risk factors in the ARIC study. Am J Epidemiol 1991;134:250-6.
2. De Silva DA, Woon FP, Lee MP, Chen CP, Chang HM, Wong MC. South Asian patients with ischemic stroke: Intracranial large arteries are the predominant site of disease. Stroke 2007;38:2592-4.
3. Psaty BM, Furberg CD, Kuller LH, Borhani NO, Rautaharju PM, O'Leary DH. Isolated systolic hypertension and subclinical cardiovascular disease in the elderly. Initial findings from the cardiovascular health study. JAMA 1992;268:1287-91.
4. Touboul PJ, Labreuche J, Vicaut E, Amarenco P, GENIC Investigators. Carotid intima-media thickness, plaques, and Framingham risk score as independent determinants of stroke risk. Stroke 2005;36:1741-5.
5. Chung JW, Park SH, Kim N, Kim WJ, Park JH, Ko Y, *et al*. Trial of ORG 10172 in acute stroke treatment (TOAST) classification and vascular territory of ischemic stroke lesions diagnosed by diffusion-weighted imaging. J Am Heart Assoc 2014;3. pii: e001119.
6. Hunt KJ, Evans GW, Folsom AR, Sharrett AR, Chambless LE, Tegeler CH, *et al.* Acoustic shadowing on B-mode ultrasound of the carotid artery predicts ischemic stroke: The atherosclerosis risk in communities (ARIC) study. Stroke 2001;32:1120-6.
7. Prati P, Tosetto A, Vanuzzo D, Bader G, Casaroli M, Canciani L, *et al.* Carotid intima media thickness and plaques can predict the occurrence of ischemic cerebrovascular events. Stroke 2008;39:2470-6.
8. Kitamura A, Iso H, Imano H, Ohira T, Okada T, Sato S, *et al.* Carotid intima-media thickness and plaque characteristics as a risk factor for stroke in Japanese elderly men. Stroke 2004;35:2788-94.
9. Cupini LM, Pasqualetti P, Diomedi M, Vernieri F, Silvestrini M, Rizzato B, *et al.* Carotid artery intima-media thickness and lacunar versus nonlacunar infarcts. Stroke 2002;33:689-94.
10. Mukherjee SC, Basu AK, Bandyopadhyay R, Pal SK, Bandopadhyay D, Mandal SK, *et al.* Correlation of lipid profile and carotid artery plaque as detected by Doppler ultrasound in ischaemic stroke patients – A hospital-based study. J Indian Med Assoc 2006;104:325-6, 330.
11. Touboul PJ, Elbaz A, Koller C, Lucas C, Adraï V, Chédru F, *et al*. Common carotid artery intima-media thickness and brain infarction: The etude du profil génétique de l'infarctus cérébral (GENIC) case-control study. The GENIC investigators. Circulation 2000;102:313-8.
12. Sahoo R, Krishna MV, Subrahmaniyan DK, Dutta TK, Elangovan S. Common carotid intima-media thickness in acute ischemic stroke: A case control study. Neurol India 2009;57:627-30.
13. Saha A, Sinha PK, Paul R, Bandyopadhyay R, Biswas K, Banerjee AK. Study of carotid intima media thickness and its correlation with novel risk factors in ischemic stroke. Neurol Asia 2011;16:25-31.
14. Hollander M, Hak AE, Koudstaal PJ, Bots ML, Grobbee DE, Hofman A, *et al.* Comparison between measures of atherosclerosis and risk of stroke: The Rotterdam study. Stroke 2003;34:2367-72.
15. Harris S. The association of carotid intima media thickness (cIMT) and stroke: A cross sectional study. New trends in neurosonology and cerebral hemodynamics – An update. Perspect Med 2012;1:164-6.