

# Prevalence and association of lifestyle factors with extracranial carotid atherosclerosis in non-cardioembolic anterior circulation strokes in adult males less than 50 years: One year cross-sectional study

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## Abstract

**Background:** Data is scarce on prevalence of extracranial carotid atherosclerosis (ECA) in strokes <50 years and its association with lifestyle factors. **Objective:** Study role of (a) ECA in non-cardio-embolic anterior circulation young strokes, and (b) smoking and alcohol in ECA. **Materials and Methods:** Cardiovascular risk factors and evidence of ECA on carotid doppler ultrasound (CDUS) was evaluated in an one-year preliminary cross-sectional study of consecutive strokes between 20 years and 49 years. Females were excluded. **Results:** There were 46 male strokes (mean age 38.26 yrs), 17.39% had hypertension, 2.23% had coronary artery disease; none was diabetic. Tobacco users and alcohol consumers were 24/46 (52.17%) cases each. ECA was found in 14/46 (30.44%) cases. Seven of these 14 (50%) i.e., 7/46 cases (15.21%) had carotid occlusion, four had <50%, three had >70% stenosis. 'Smoking and smokeless tobacco use' was found in 71.42% (10/14) symptomatic carotid lesions compared to 43.75% (14/32) strokes without carotid lesions. Prevalence odds ratio for tobacco use and ECA was 3.21 (95% CI: 0.83-12.44) while that of alcohol and ECA was 1.33 (95% CI: 0.38-4.72). **Conclusion:** Prevalence of ECA in strokes <50 years was high due to lifestyle factors which predispose to atherosclerosis at younger age.

## Key Words

Alcohol, extracranial carotid atherosclerosis, lifestyle factors, smoking, young stroke

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## Introduction

Stroke in young has emerged as a major public health problem in India. The prevalence of stroke in younger individuals is high (18-32% of all stroke cases) compared with high income countries.<sup>[1]</sup> The causes of stroke in young are more varied and even after extensive investigations remain elusive in 20-50% of young patients.<sup>[2]</sup> While the age group included in studies on stroke varies widely in the reports published in literature, it has been recommended that future studies should consider keeping 15-49 years (<50 years) as the age group for studies on stroke in young.<sup>[3]</sup>

Diabetes mellitus, hypertension, heart disease, current smoking, and long-term heavy alcohol consumption are major risk factors for stroke in young adults as in elder population.<sup>[3,4]</sup> Recent data from several studies indicate that 21-48% of strokes in young are caused by atherosclerotic large artery occlusive disease.<sup>[3]</sup> However, there is paucity of data on the role of extracranial carotid atherosclerosis (ECA) and its association with lifestyle factors like smoking and alcohol use in causation of ischemic stroke in younger age group. Perhaps, there is no exclusive data available on this subject from the Indian sub-continent. The present study looks at the association of smoking and alcohol in causation of ECA as a cause of stroke in young.

## Materials and Methods

This cross-sectional preliminary observational study was conducted at Armed Forces Medical College (AFMC)-Command Hospital, Pune from 02 March 2009 to 16 Feb 2010. The study aimed to investigate (a) the prevalence of ECA, and (b) to study the association of premature carotid atherosclerosis

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with lifestyle factors like smoking and alcohol amongst patients with first anterior circulation ischemic stroke in age group 20-49 years. Exclusion criteria included (a) posterior circulation strokes, (b) likely cardio-embolic strokes due to valvular heart disease, cardiomyopathy, atrial fibrillation, and heart failure, and (c) female strokes. As we intended to study the impact of lifestyle factors in stroke, females were excluded as smoking and alcohol consumption by females is not a universal habit in conventional Indian society. Eligible patients enrolled in the study belonged to different parts and ethnic races of India.

Patients were screened for modifiable and non-modifiable vascular risk factors. Smoker was defined as a person having 1 or more pack years of smoking (1 pack = 20 cigarettes). Tobacco chewers were included in the smokers category as they have been referred to as 'smokeless tobacco users' with similar cardiovascular risk potential.<sup>[5]</sup> Regular alcohol consumer was defined as a person with alcohol consumption >70 grams/week.<sup>[6]</sup> Alcohol consumption <70 grams/week or occasional consumption was taken as non-alcohol consumer. In addition, we collected data for hypertension, diabetes mellitus, heart disease, and presence of hypercholesterolemia.

All patients were subjected to routine hematological and metabolic workup, electrocardiogram (ECG), echocardiography, magnetic resonance imaging of brain, magnetic resonance angiography of intracranial and extracranial vessels, and carotid doppler ultrasonography (CDUS). Workup for vasculitis, anti-phospholipid antibody, and prothrombotic factors was done in cases when patient could afford the tests. All patients gave informed consent to participate in the study.

The study variables included presence of stenosis, degree of stenosis (high-grade >70%, moderate 50-70% and low grade <50%) and whether the site of abnormality corresponded to the clinical deficit. Measurement of intima media thickness and characterization of plaque was not analyzed, these variables being highly observer dependant and data having been inconsistently recorded.

Data was analyzed for prevalence of ECA in this subset of stroke patients. We dichotomized current smoking (yes/no) and current alcohol consumption (yes/no) to evaluate their association with ECA. The statistical analysis was done using R 2.15.1 software.<sup>[7]</sup>

## Results

A total of 46 consecutive male patients met the eligibility criteria with age ranging from 20 yrs to 49 yrs (mean age 38.26 yrs) with 26 (56.52%) patients between ages 40 yrs and 49 yrs. Twenty-six had left hemispheric stroke while 20 had right hemispheric stroke. There were eight (three known, five diagnosed first-time) (17.39%) patients with hypertension, one (2.17%) had coronary artery disease (CAD), and none had diabetes mellitus or peripheral arterial disease. There were 24 (52.17%) tobacco users (20 smokers and four smokeless tobacco users) and 22 (47.83%) tobacco non-users. There were 24 (52.17%) regular alcohol consumers and 22 (47.83%) non-alcohol consumers. Of

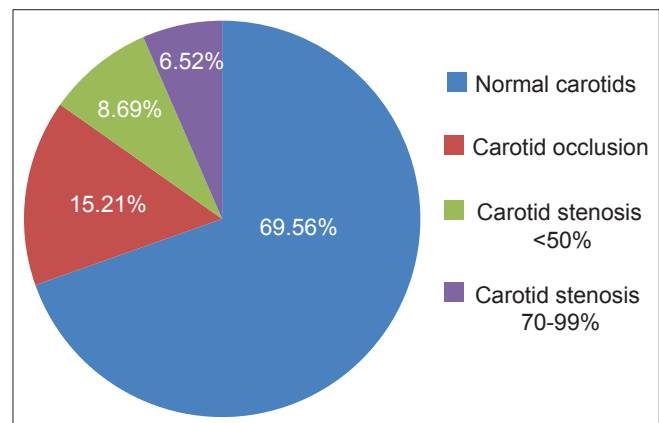
the eight cases with hypertension, three (37.5%) were neither tobacco users nor alcohol consumers, while four (50%) were both tobacco users and alcohol consumers, and one (12.5%) was only tobacco user; all the alcohol consumers were tobacco users with >20 pack years.

Hemogram, metabolic parameters, and ECG were normal in all patients. Echocardiography was normal in 32 cases, and showed patent foramen ovale and ventricular hypertrophy in two cases each; it was not available for 10 cases. Of 35 patients for whom low-density lipoprotein (LDL) cholesterol was available, nine patients had LDL cholesterol >100 mg/dl. Of these nine patients, three had carotid artery stenosis, one had carotid occlusion, while five had normal carotid arteries.

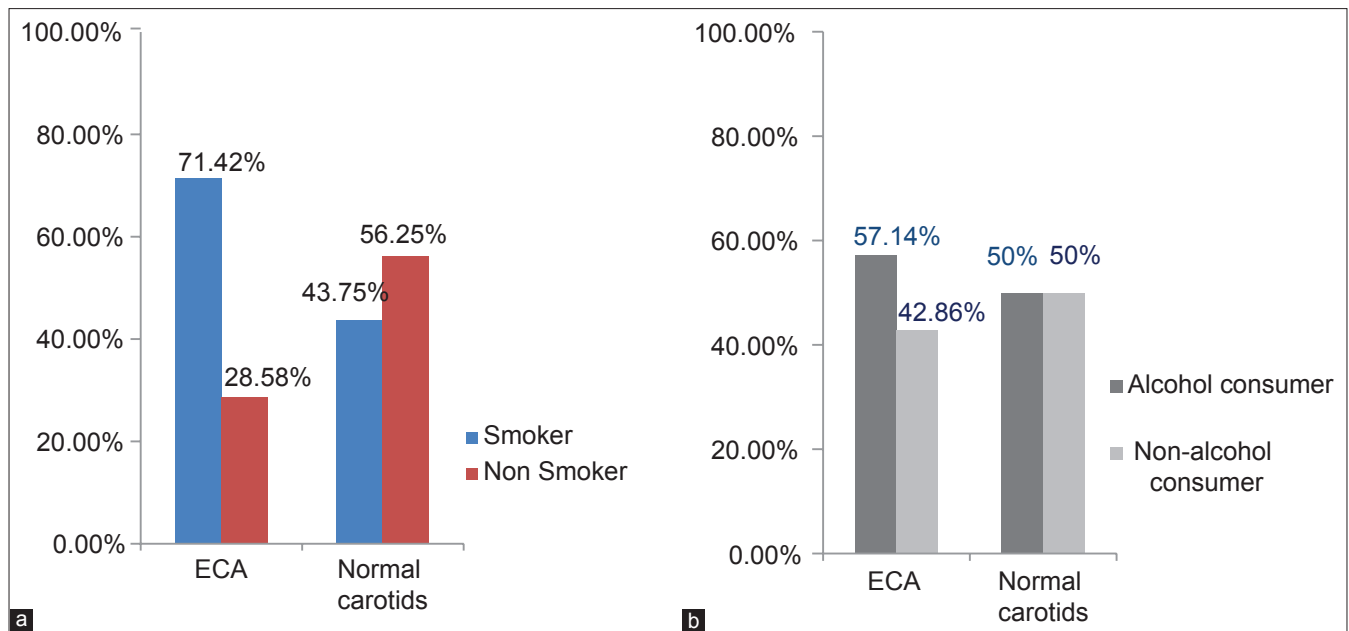
The CDUS examination found atherosclerotic plaque/occlusion on symptomatic side in 14 of the 46 (30.44%) patients. Seven of these 14 cases (50%) i.e. seven of 46 cases (15.21%) had carotid occlusion, four had <50% stenosis, while three had >70% stenosis [Figure 1]. The CDUS examination was normal in 32 of the 46 patients (69.56%). In all of these patients with carotid stenosis, the clinical deficit corresponded to the territory of the infarct.

There were 24 of 46 (52.17%) strokes which occurred in 'smokers and smokeless tobacco users', while 22 of 46 (47.83%) strokes occurred in non-smokers. There were 10 of 14 (71.42%) symptomatic carotid lesions which were associated with 'smoking and smokeless tobacco use'; 14 of 32 (43.75%) strokes without carotid lesions were associated with 'smoking and smokeless tobacco use' [Figure 2a]. The prevalence odds ratio (OR) for tobacco use and ECA was 3.21 (95% CI: 0.83-12.44).

There were 24 of 46 (52.17%) strokes which occurred in regular alcohol consumers, while 22 of 46 (47.83%) strokes occurred in non-alcohol consumers. There were eight of 14 (57.14%) symptomatic carotid lesions which were associated with alcohol consumption; 16 of 32 (50%) of stroke without carotid lesions were associated with alcohol consumption [Figure 2b]. The prevalence OR for alcohol consumption and ECA was 1.33 (95% CI: 0.38-4.72).



**Figure 1: Extracranial carotid atherosclerosis in 14 of 46 (30.44%) cases, carotid occlusion in 7 of 14 (50%) i.e. 7 of 46 (15.21%) cases, carotid stenosis <50% in 4 (8.69%) cases, carotid stenosis >70% in 3 (6.52%) cases, and normal carotids in 32 of 46 (69.56%) cases**



**Figure 2: 10 of 14 (71.42%) cases with extracranial carotid atherosclerosis were smokers and 14 of 32 (43.75%) cases with normal carotids were smokers (a), 8 of 14 (57.14%) cases of extracranial carotid atherosclerosis were alcohol consumers and 16 of 32 (50%) cases with normal carotids were alcohol consumers (b)**

In this study of strokes less than 50 years we found that there was a greater association of smoking with ECA as compared to alcohol.

## Discussion

The incidence of stroke in young is higher in the Indian subcontinent than the west but precise causes are not known. In an angiographic study, primary atherosclerosis was thought to be the cause of young stroke in Indian population.<sup>[8]</sup>

Smoking was observed in 44% patients and males were more often heavy drinkers in Helsinki Stroke Study.<sup>[9]</sup> Previous studies have shown alcohol and smoking as important risk factors.<sup>[4,10-12]</sup> Cigarette smoking is a traditional risk factor for atherosclerosis and previous studies have demonstrated positive association with carotid intima media thickness and increased risk of atherosclerosis.<sup>[13]</sup> However, little is known about alcohol consumption and carotid atherosclerosis. Both smoking and alcohol consumption are modifiable cardiovascular risk factors and offer potential for primary and secondary preventions of stroke.<sup>[13]</sup>

We present our preliminary observation with CDUS in 46 patients with anterior circulation non-cardio-embolic strokes aged 20-49 years. Non-modifiable cardiovascular risk factors for atherosclerosis were found in relatively smaller proportion of cases: 25.17% had raised LDL-cholesterol, 17.39% had hypertension, 2.23% had cardiovascular disease, none had diabetes mellitus, which compares with figures of 42%, 39%, 10.2%, 10.4%, respectively, in similar age group in the Helsinki Young Stroke Registry.<sup>[9]</sup> In this study, there were 62.5% cases of hypertension with lifestyle risk factors, 50% of these having both risk factors.

Large artery atherosclerosis was seen in 8% of strokes under 50 years in the Helsinki young stroke registry,<sup>[9]</sup> while it was reported in 21% of ischemic strokes aged between 15 years and 44 years from Korea.<sup>[14]</sup> Large artery atherosclerosis was 26.9% and 41% of strokes in all age groups in two separate studies from Indian subcontinent.<sup>[15,16]</sup> The Indian study found intracranial rather than extracranial large artery atherosclerosis to be more common in strokes.<sup>[16]</sup> We did not find intracranial atherosclerosis perhaps this being more common in females and in older age group in the subcontinent.

We found 31% ischemic strokes <50 years with ECA nearly half of whom had carotid occlusion, which is at variance with the foregoing studies from the Indian sub-continent. We did not find intracranial atherosclerotic disease in our series. The high rate of ECA in this series is commensurate with the increasing prevalence of lifestyle factors for atherosclerosis, and highlights the recurrent theme of atherosclerotic disease in stroke in this study.

Increased wall thickness of carotid arteries and increased prevalence of carotid atherosclerotic lesions/thrombotic occlusions in young strokes with relatively low incidence of cardiovascular risk factors have been reported from Italy.<sup>[17]</sup> This is in keeping with findings from our study. The arterial intima-media thickness is an important determinant of vascular disease in young patients. There may be potential role of genetic factors in the genesis of atherosclerosis in the young.<sup>[17]</sup>

Stroke risk is greatly increased in presence of cigarette smoking.<sup>[18]</sup> The magnitude of association of smoking is substantial compared with other traditional cardiovascular risk factors in the age group 55-70 years.<sup>[19]</sup> A positive relation between smoking and carotid artery disease has been found

in older adults.<sup>[20]</sup> In these studies, smoking did not seem to predispose to stroke in older patients in absence of carotid atherosclerotic disease.

However, there are no similar studies on association of smoking and ECA in younger age group. Our study found a positive relation between smoking/smokeless tobacco use and ECA (71.42%), whereas only 43.75% of strokes without ECA were associated with smoking. The OR of 3.21 (95% CI: 0.83-12.44) shows trend toward association between smoking and formation of extracranial carotid plaques.

In a study from Bangladesh, up to 79.7% cases of CAD among young patients aged 20-49 years were either current or past consumers of some form of tobacco, compared with less than half of the controls (46.4%).<sup>[5]</sup> As vascular risk factors are common for CAD and cerebrovascular disease, our preliminary study compares well with the study on young CAD from Bangladesh, and this may have relevance for larger study on this aspect of young strokes in India.

There is a U-shaped association of alcohol intake and ischemic stroke in white population. The net effect of alcohol has been found to be a positive predictor of carotid atherosclerosis.<sup>[6]</sup> In our study, though only slightly greater proportion of strokes occurred in alcohol consumers but the OR of 1.33 (95% CI: 0.38-4.72) may implicate alcohol as associated with formation of carotid plaques. Alcohol may perhaps also contribute to stroke through mechanisms other than carotid atherosclerosis.

Smoking was found to be more important risk factor for stroke than alcohol in elderly population from Taiwan,<sup>[21]</sup> as has been found in this study of younger ischemic strokes from India. Smoking and genetic polymorphism of apolipoprotein E has been found to have synergistic effects on prevalence of carotid atherosclerosis independent of LDL cholesterol.<sup>[13]</sup> An association between smoking and carotid atherosclerosis after adjustment for LDL and high-density lipoprotein (HDL) cholesterol has been found suggesting that mechanisms other than lipids may play a role in atherosclerosis. This particular subgroup, similar to our patient series, may benefit from preventive measures.<sup>[13]</sup>

Although, several prior reports have earlier associated the metabolic syndrome with stroke risk in middle aged to older adults, such an association in young strokes was reported for first time in a study from South India which found strong association of the conjoint presence of multiple components of metabolic syndrome with stroke in young adults.<sup>[11]</sup> Non-modifiable cardiovascular risk factors did not seem to be important causes of stroke in this younger age group of ischemic strokes. In this select cohort of non-cardio-embolic anterior circulation ischemic strokes under 50 years, 30.44% had ECA possibly attributed to lifestyle factors. Similar finding has not been reported earlier from India.

The study has some shortcomings. As the lower value of 95% CI for OR for both smoking and alcohol is lower than one due to small sample size, these variables were not significantly associated with ECA. As we did not study individuals without stroke, we can only infer the prevalence of these variables in this select population.

## Conclusion

This study highlights the importance of ECA as a major cause of stroke in young adults. The high prevalence of lifestyle factors like smoking and alcohol points to the need for early prevention. It also provides physicians with an impetus to use CDUS as a routine diagnostic and management modality in young stroke patients. This may enable early treatment to make a significant impact on the natural history of this disease. The data also provides opportunity to study the potential role of genetic factors in causation of atherosclerosis in young.

We postulate that smoking more than alcohol is associated with higher prevalence for ECA, and alcohol perhaps contributes to stroke through mechanisms other than carotid atherosclerosis. A larger cohort study from Indian sub-continent is required on the basis of this preliminary cross-sectional study to establish the causative role of smoking and alcohol in ECA in young strokes with paucity of other cardiovascular risk factors.

## References

1. "Das SK, Banerjee TK. Stroke: Indian Scenario. *Circulation* 2008;118:2719-24."
2. Sanchette P. Stroke in Young. Editorial. *J Indian Acad Clin Med* 2002;3:228-30.
3. Prasad K, Singhal KK. Stroke in young: An Indian perspective. *Neural India* 2010;58:343-50.
4. Lee TH, Hsu WC, Chen CJ, Chen ST. Etiologic study of young ischemic stroke in Taiwan. *Stroke* 2002;33:1950-5.
5. Rahman M, Zaman M. Smoking and smokeless tobacco consumption: Possible risk factors for coronary heart disease among young patients attending a tertiary care cardiac hospital in Bangladesh. *Public Health* 2008;122:1331-8.
6. Kiechl S, Willeit J, Rungger G, Egger G, Oberhollenzer F, Bonora E. Alcohol consumption and atherosclerosis: What is the relation? Prospective results from the bruneck study. *Stroke* 1998;29:900-7.
7. R Core Team (2012). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Available from: <http://www.R-project.org/> [Last accessed date on 31 May 2013].
8. Jayakumar PN, Taly AB, Arya BY, Nagaraja D. Angiographic profile of ischaemic stroke in the young-study of 143 cases. *Clin Radiol* 1991;44:236-9.
9. Putaala J, Metso AJ, Metso TM, Konkola N, Kraemer Y, Haapaniemi E, *et al.* Analysis of 1008 consecutive patients aged 15 to 49 with first-ever ischemic stroke: The Helsinki Young Stroke Registry. *Stroke* 2009;40:1195-203.
10. Nayak SD, Nair M, Radhakrishnan K, Sarma PS. Ischemic stroke in the young adult: Clinical features, risk factors and outcome. *Natl Med J India* 1997;10:107-12.
11. Lipska K, Sylaja PN, Sarma PS, Thankappan Kr, Kutty VR, Vasani RS, *et al.* Risk factors for acute ischemic stroke in young adults in South India. *J Neurol Neurosurg Psychiatry* 2007;78:959-63.
12. Nedeltchev K, der Maur TA, Georiadis D, Arnold M, Caso V, Mattie HP, *et al.* Ischemic stroke in young adults: Predictors of outcome and recurrence. *J Neurol Neurosurg Psychiatry* 2005;76:191-5.
13. Djoussé L, Myers RH, Province MA, Hunt SC, Eckfeldt JH, Evans G, *et al.* Influence of apolipoprotein E, smoking, and alcohol intake on carotid atherosclerosis: National Heart, Lung, and Blood Institute Family Heart Study. *Stroke* 2002;33:1357-61.
14. Kwon SU, Kim JS, Lee JH, Lee MC. Ischaemic stroke in Korean young adults. *Acta Neurol Scand* 2000;101:19-24.
15. Syed NA, Khealani BA, Ali S, Hasan A, Akhtar N, Brohi H, *et al.*

- Ischemic stroke subtypes in Pakistan: The Aga Khan University Stroke Data Bank. *J Pak Med Assoc* 2003;53:584-8.
16. Kaul S, Sunitha P, Suvama A, Meena AK, Uma M, Reddy JM. Subtypes of Ischemic Stroke in a Metropolitan City of South India (One year data from a hospital based stroke registry). *Neurol India* 2002;50 Suppl: S8-14.
  17. Oliviero U, Orefice G, Coppola G, Scherillo G, Ascione S, Casaburi C, *et al.* Carotid atherosclerosis and ischemic stroke in young patients. *Int Angiol* 2002;21:117-22.
  18. Bevan H, Sharma K, Bradley W. Stroke in young adults. *Stroke* 1990;21:382-6.
  19. Howard G, Wagenknecht LE, Cai J, Cooper L, Kraut MA, Toole JF. Cigarette smoking and other risk factors for silent cerebral infarction in the general population. *Stroke* 1998;29:913-7.
  20. Tell GS, Polak JF, Ward BJ, Kittner SJ, Savage PJ, Robbins J. Relation of smoking with carotid artery wall thickness and stenosis in older adults. The Cardiovascular Health Study. The Cardiovascular Health Study (CHS) Collaborative Research Group. *Circulation* 1994;90:2905-8.
  21. Lee TK, Huang ZS, Ng SN, Chan KW, Wang YS, Liu HW, *et al.* Impact of alcohol consumption and cigarette smoking on stroke among the elderly in Taiwan. *Stroke* 1995;26:790-4.

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