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Original Research Article

SMOKING STATUS AND MIDDLE CEREBRAL ARTERY TERRITORY INFARCTION IN ACUTE ISCHEMIC STROKE: A HOSPITAL-BASED CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Smoking is a known modifiable risk factor for acute ischemic stroke. Its association with the radiological territory of infarction is less frequently assessed in routine hospital-based Indian studies. The present study assessed the association between smoking status and middle cerebral artery territory infarction in patients with acute ischemic stroke.

Material and Methods: This hospital-based cross-sectional study included 110 adult patients with radiologically confirmed acute ischemic stroke. Patients were classified as smokers and non-smokers. Baseline profile, vascular risk factors, infarct territory, stroke severity by National Institutes of Health Stroke Scale and discharge outcome by modified Rankin Scale were recorded. Fisher's exact test was used to assess the association between smoking and MCA territory infarction. Odds ratio, risk ratio and risk difference with 95% confidence interval were calculated.

Results: Of 110 patients, 31 (28.2%) were smokers and 79 (71.8%) were non-smokers. Mean age was 63.1 +/- 10.6 years. Male patients were 71 (64.5%). Hypertension was the most common vascular risk factor and was present in 71 patients (64.5%). Dyslipidaemia and alcohol use were significantly more frequent among smokers. MCA territory infarct was seen in 28 smokers (90.3%) and 53 non-smokers (67.1%). Smoking was significantly associated with MCA territory infarct by Fisher's exact test (OR 4.58, 95% CI 1.27 to 16.46; p=0.015). The risk ratio was 1.35 and the absolute risk difference was 23.2%.

Conclusion: Smoking was associated with a higher proportion of MCA territory infarction in patients with acute ischemic stroke. The finding supports smoking as an important modifiable vascular risk marker. Larger studies with pack-year assessment, vascular imaging and adjusted analysis are required.

Keywords: Acute ischemic stroke, Smoking, Middle cerebral artery, Infarct territory, Vascular risk factors, NIHSS.

INTRODUCTION

Stroke remains a major cause of death and long-term disability worldwide.[1] In India also, stroke contributes substantially to mortality and disability-adjusted life years, with variation across different states and regions.[2] Acute ischemic stroke is a common clinical presentation in hospital practice. Early assessment of vascular risk factors and infarct territory is important for clinical classification and risk reduction.

Smoking is an important modifiable risk factor for acute stroke.[3] The INTERSTROKE analysis from 32 countries reported a clear association between current smoking and acute stroke risk.[3] Smoking produces vascular injury through endothelial dysfunction, oxidative stress, inflammation, platelet activation and accelerated atherosclerosis.[4] These mechanisms can promote thrombus formation and

large artery disease. Infarct territory gives useful radiological information in acute ischemic stroke. The middle cerebral artery is the most commonly involved artery in acute stroke because it supplies a large vascular territory and arises as a major continuation from the internal carotid system.[5] MCA territory infarction is clinically important as it can involve motor, sensory, speech and cortical functions. Indian hospital-based studies commonly report hypertension, diabetes mellitus, dyslipidaemia, alcohol intake and smoking as major vascular risk factors among stroke patients.[6,7] Smoking often coexists with other risk factors. Therefore, comparison of smokers and non-smokers should include baseline profile, vascular risk factors, infarct site and stroke severity.

Data regarding smoking and specific infarct territory are still limited in routine Indian hospital settings. The present study was planned to assess the association between smoking status and radiological infarct territory in patients with acute ischemic stroke, with special focus on MCA territory infarction.

MATERIALS AND METHODS

Study design and setting

This was a hospital-based cross-sectional study conducted in the Department of General Medicine at a tertiary care teaching hospital in India. The study included adult patients admitted with acute ischemic stroke during the defined study period.

Study population

Adult patients aged 18 years and above with radiologically confirmed acute ischemic stroke were included. Stroke diagnosis was confirmed by computed tomography or magnetic resonance imaging of brain. Patients were grouped into smokers and non-smokers based on documented smoking history.

Inclusion Criteria

- Age 18 years and above.
- Radiologically confirmed acute ischemic stroke.
- Availability of smoking history.
- Availability of clear infarct territory on CT or MRI.

Exclusion Criteria

- Hemorrhagic stroke.
- Transient ischemic attack without radiological infarct.
- Incomplete smoking history.
- Unclear or non-classifiable infarct territory.
- Patients with incomplete core clinical data.

Study variables

The main exposure variable was smoking status. The main outcome variable was MCA territory infarction. Other variables included age, sex, time from symptom onset to imaging, hypertension, diabetes mellitus, dyslipidaemia, alcohol use, previous stroke, atrial fibrillation, infarct territory, NIHSS severity category, hospital stay and discharge outcome by modified Rankin Scale.

Operational definitions

Smokers were defined as patients with a documented history of current or previous smoking. Non-smokers were patients without any documented smoking history. MCA territory infarct included infarcts localized radiologically to the middle cerebral artery territory. Non-MCA infarcts included ACA, PCA, brainstem and cerebellar infarcts. Good discharge outcome was defined as mRS 0-2. Poor discharge outcome was defined as mRS 3-6.

Statistical Analysis

Data were entered in Microsoft Excel and analysed using statistical software. Continuous variables were expressed as mean +/- standard deviation or median with interquartile range. Categorical variables were expressed as frequency and percentage. Welch t-test was used for comparison of age between smokers and non-smokers. Fisher's exact test was used for categorical variables and for the primary association between smoking and MCA territory infarction. Odds ratio, risk ratio and risk difference with 95% confidence interval were calculated. A p value <0.05 was considered statistically significant.

RESULTS

A total of 110 patients with radiologically confirmed acute ischemic stroke were included. Thirty-one patients (28.2%) were smokers and 79 patients (71.8%) were non-smokers. The mean age of the study population was 63.1 +/- 10.6 years. Mean age was 60.9 +/- 9.8 years among smokers and 64.0 +/- 10.9 years among non-smokers. The age difference was not statistically significant (p=0.154). Male patients were significantly more frequent among smokers than non-smokers (93.5% versus 53.2%; p<0.001).

Table 1: Baseline profile of study participants

Variable	Smokers n=31	Non-smokers n=79	Total n=110	p value
Age, years, mean +/- SD	60.9 +/- 9.8	64.0 +/- 10.9	63.1 +/- 10.6	0.154
Male sex	29 (93.5%)	42 (53.2%)	71 (64.5%)	<0.001
Female sex	2 (6.5%)	37 (46.8%)	39 (35.5%)	—
Symptom onset to imaging <24 hours	20 (64.5%)	46 (58.2%)	66 (60.0%)	0.666
Symptom onset to imaging >=24 hours	11 (35.5%)	33 (41.8%)	44 (40.0%)	—

Hypertension was the most common vascular risk factor and was present in 71 patients (64.5%). Diabetes mellitus was present in 40 patients (36.4%). Dyslipidaemia and alcohol use were significantly more frequent among smokers. Dyslipidaemia was present in 48.4% of smokers and 21.5% of non-smokers (p=0.009). Alcohol use was present in 58.1% of smokers and 21.5% of non-smokers (p<0.001).

Table 2: Vascular risk factors among smokers and non-smokers

Variable	Smokers n=31	Non-smokers n=79	Total n=110	p value
Hypertension	20 (64.5%)	51 (64.6%)	71 (64.5%)	1.000
Diabetes mellitus	11 (35.5%)	29 (36.7%)	40 (36.4%)	1.000
Dyslipidaemia	15 (48.4%)	17 (21.5%)	32 (29.1%)	0.009
Alcohol use	18 (58.1%)	17 (21.5%)	35 (31.8%)	<0.001
Previous stroke	3 (9.7%)	7 (8.9%)	10 (9.1%)	1.000
Atrial fibrillation	1 (3.2%)	8 (10.1%)	9 (8.2%)	0.441

MCA territory infarct was the most common infarct pattern and was seen in 81 patients (73.6%). MCA involvement was present in 28 smokers (90.3%) and 53 non-smokers (67.1%). ACA territory infarct was seen in 11 patients (10.0%), PCA territory infarct in 13 patients (11.8%) and brainstem/cerebellar infarct in 5 patients (4.5%).

Table 3: Radiological infarct territory by smoking status

Infarct territory	Smokers n=31	Non-smokers n=79	Total n=110
MCA territory	28 (90.3%)	53 (67.1%)	81 (73.6%)
ACA territory	1 (3.2%)	10 (12.7%)	11 (10.0%)
PCA territory	2 (6.5%)	11 (13.9%)	13 (11.8%)
Brainstem/cerebellum	0 (0.0%)	5 (6.3%)	5 (4.5%)

For primary analysis, infarct territory was grouped as MCA infarct and non-MCA infarct. MCA infarct was seen in 28 out of 31 smokers (90.3%) compared with 53 out of 79 non-smokers (67.1%). Smoking was associated with higher odds of MCA territory infarct by Fisher's exact test (OR 4.58, 95% CI 1.27 to 16.46; p=0.015). The risk ratio was 1.35 and the absolute risk difference was 23.2%.

Table 4A: Association between smoking and MCA territory infarct

Infarct pattern	Smokers n=31	Non-smokers n=79	Total n=110
MCA infarct	28 (90.3%)	53 (67.1%)	81 (73.6%)
Non-MCA infarct	3 (9.7%)	26 (32.9%)	29 (26.4%)

Table 4B: Effect estimates for MCA territory infarct

Measure	Value
Fisher's exact p value	0.015
Odds ratio	4.58
95% CI for odds ratio	1.27 to 16.46
Risk ratio	1.35
95% CI for risk ratio	1.11 to 1.63
Risk difference	23.2%
95% CI for risk difference	8.5% to 37.9%

Moderate stroke severity was the most frequent NIHSS category and was seen in 54 patients (49.1%). Mild stroke was seen in 34 patients (30.9%) and severe stroke in 22 patients (20.0%). Poor discharge outcome was seen in 39 patients (35.5%). Poor outcome was more frequent among smokers than non-smokers, 41.9% versus 32.9%.

Table 5: Stroke severity and discharge outcome

Variable	Smokers n=31	Non-smokers n=79	Total n=110
NIHSS <=5, mild stroke	6 (19.4%)	28 (35.4%)	34 (30.9%)
NIHSS 6-15, moderate stroke	18 (58.1%)	36 (45.6%)	54 (49.1%)
NIHSS >15, severe stroke	7 (22.6%)	15 (19.0%)	22 (20.0%)
Hospital stay, days, median IQR	6 (5-8)	5 (4-7)	5 (4-7)
Good outcome, mRS 0-2	18 (58.1%)	53 (67.1%)	71 (64.5%)
Poor outcome, mRS 3-6	13 (41.9%)	26 (32.9%)	39 (35.5%)

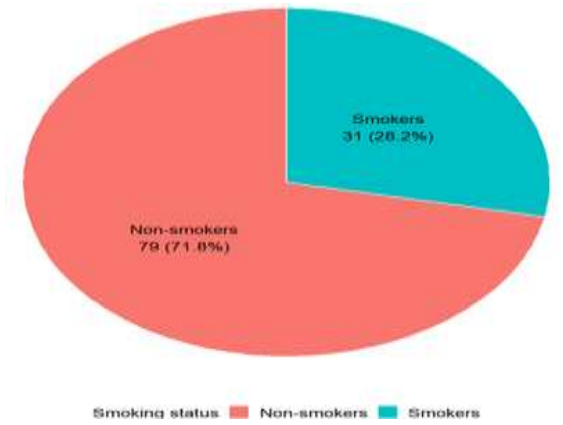

Figure 1: Distribution of smoking status among acute ischemic stroke patients

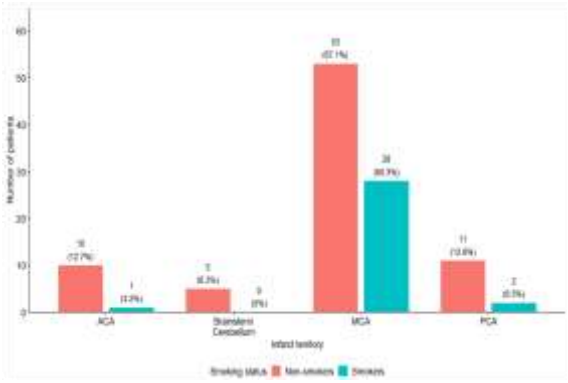

Figure 2: Infarct territory distribution among smokers and non-smokers

DISCUSSION

In the present study, smokers constituted 31 patients (28.2%) among 110 patients with acute ischemic stroke. This is in line with Indian pooled stroke data where tobacco use was reported in nearly one-third of stroke patients.[6] In the Indo-US Collaborative Stroke Project, 2066 ischemic stroke patients were studied across five high-volume tertiary centres in India and tobacco use was a common vascular risk factor.[7] Thus, the smoking proportion in the present study appears comparable to Indian hospital-based stroke populations. Male predominance was marked among smokers. Male sex was seen in 29 smokers (93.5%) compared with 42 non-smokers (53.2%). This difference was statistically significant. Indian stroke studies have commonly shown male predominance among admitted stroke patients.[6,7]

In our study also, males formed 64.5% of the total sample. The stronger male clustering in smokers is important because sex itself may act as a confounder in smoking-related stroke analysis.

Hypertension was the most common vascular risk factor in this study and was present in 71 patients (64.5%). This agrees with Indian stroke literature. Varkey et al. reported hypertension as the most frequent lifestyle and clinical risk factor in Indian stroke studies.[6] Sylaja et al. also reported hypertension and diabetes as major comorbidities in Indian ischemic stroke patients.[7] In our study, diabetes mellitus was present in 40 patients (36.4%). This pattern is consistent with routine Indian tertiary care stroke data. Dyslipidaemia was present in 32 patients (29.1%). This was significantly more common among smokers than non-smokers, 48.4% versus 21.5%. Alcohol use was also significantly higher among smokers, 58.1% versus 21.5%. This clustering is clinically relevant. It suggests that smoking status may represent a broader adverse vascular risk profile. Therefore, the observed association between smoking and MCA territory infarction should be interpreted with this background.

The main finding of this study was the higher proportion of MCA territory infarct among smokers. MCA territory infarct was present in 28 out of 31 smokers (90.3%) and 53 out of 79 non-smokers (67.1%). Smoking showed a significant association with MCA territory infarction by Fisher's exact test. The odds ratio was 4.58 with 95% CI 1.27 to 16.46. The risk ratio was 1.35 and the absolute risk difference was 23.2%. This means that MCA infarct was not only statistically more frequent among smokers but also had a clinically meaningful difference in proportion. The association is biologically plausible. Smoking is linked with endothelial dysfunction, oxidative stress, platelet activation and accelerated atherosclerosis.[4] Pan et al. in a meta-analysis reported that smokers had higher odds of stroke compared with non-smokers, with pooled OR 1.6.[11] Luo et al. also reported that the risk of different pathological types of stroke was higher among smokers and showed dose-response relation.[12] Bhat et al. reported a strong dose-response relationship between cigarette smoking and ischemic stroke risk in young women.[13] These studies support the harmful vascular role of smoking in ischemic stroke.

The predominance of MCA infarction among smokers may reflect large artery involvement. MCA is one of the most commonly involved arteries in acute stroke because of its large territory and direct relation with the internal carotid circulation [5]. Smoking can accelerate carotid and intracranial atherosclerosis. However, our study did not include carotid Doppler, CT angiography, MR angiography or TOAST classification. Therefore, the mechanism cannot be confirmed from this dataset. It is safer to state that smoking was associated with MCA territory infarction rather than that smoking directly caused MCA infarction. Some Indian studies on young ischemic stroke also support the relevance of smoking. Lipska et al. reported smoking as a strong risk factor for acute ischemic stroke in young adults in South India.[9] Moond et al. reported hypertension, dyslipidaemia and smoking as common risk factors in young Indian ischemic stroke patients.[10] These findings support the role of smoking in stroke pathogenesis in Indian populations. However, these studies examined stroke risk and risk factor profile. They did not

specifically establish smoking as a determinant of MCA territory infarction.

The present study also looked at severity and discharge outcome. Moderate stroke severity was most common and was seen in 54 patients (49.1%). Poor discharge outcome was seen in 39 patients (35.5%). Poor outcome was more frequent among smokers than non-smokers, 41.9% versus 32.9%. This is a descriptive finding only. It was not the primary outcome and no adjusted analysis was done for this outcome. Still, it supports the need to consider stroke severity and functional status along with infarct site.

Some published literature gives opposing or mixed results regarding smoking and stroke outcome. Li et al. concluded in a systematic review and meta-analysis that the so-called smoking paradox is not true in ischemic stroke patients and smokers develop ischemic stroke at a younger age.[14] Kurmann et al. found that better unadjusted outcome in smokers after thrombolysis was mainly related to baseline differences and not to a biological benefit of smoking.[15] Von Martial et al. reported outcome differences after endovascular treatment but cautioned against interpreting smoking as beneficial.[16] Zhao et al. reported that smoking in mechanical thrombectomy patients may be related to worse in-hospital and functional outcomes in some subgroups.[17] Wang et al. also showed that smokers had about two-fold stroke mortality and longer disability burden.[18] These studies oppose any protective interpretation of smoking. The present study has a few strengths. It used radiologically confirmed acute ischemic stroke. It compared smokers and non-smokers using infarct territory. It also included vascular risk factors, NIHSS severity and discharge outcome. The effect size was presented by odds ratio, risk ratio and risk difference, not only by p value. This improves clinical interpretation.

There are important limitations. The study was hospital-based and may not represent the community. Smoking was classified as present or absent and pack-years were not analysed. Current and former smokers were not separated. Bidi, cigarette and smokeless tobacco exposure were not studied separately. Vascular imaging data were not included. The analysis was not adjusted for male sex, dyslipidaemia, alcohol use, hypertension duration, diabetes control or atrial fibrillation. Hence, causality cannot be inferred. The study showed that MCA territory infarction was significantly more common among smokers than non-smokers. The result is consistent with the known vascular effects of smoking and with Indian stroke risk factor data. However, because smoking clustered with male sex, dyslipidaemia and alcohol use, the finding should be interpreted as an association. Larger Indian studies with pack-year analysis, vascular imaging and multivariable adjustment are required.

CONCLUSION

Smoking was significantly associated with higher proportion of MCA territory infarction in acute ischemic stroke patients. Smokers had higher odds and risk of MCA involvement than non-smokers. Dyslipidaemia and alcohol use were also more frequent among smokers, so smoking may also represent a high-risk vascular and lifestyle profile. However, this was a single-centre hospital-based study and smoking exposure was not quantified by pack-years. Current and former smokers were not analysed separately and bidi, cigarette and smokeless tobacco use were not separated. Vascular imaging and TOAST subtype were not included and no multivariable adjustment was done for sex, dyslipidaemia, alcohol use and other confounders. Discharge outcome was only descriptive. Therefore, the findings should be taken as an association, not direct causation. Larger studies with pack-year assessment, vascular imaging and adjusted analysis are required.

REFERENCES

1. Feigin VL, Abate MD, Abate YH, Abd ElHafeez S, Abd-Allah F, Abdelalim A, et al. Global, regional and national burden of stroke and its risk factors, 1990-2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Neurol. 2024;23(10):973-1003. doi:10.1016/S1474-4422(24)00369-7.
2. Behera DK, Rahut DB, Padma VM, Dash S. Analyzing stroke burden and risk factors in India using data from the Global Burden of Disease Study. Sci Rep. 2024;14(1):22640. doi:10.1038/s41598-024-72551-4.
3. Wang X, Liu X, O'Donnell MJ, et al. Tobacco use and risk of acute stroke in 32 countries in the INTERSTROKE study: a case-control study. EClinicalMedicine. 2024;70:102515. doi:10.1016/j.eclinm.2024.102515.
4. Ishida M, Sakai C, Kobayashi Y, Ishida T. Cigarette smoking and atherosclerotic cardiovascular disease. J Atheroscler Thromb. 2024;31(3):189-200. doi:10.5551/jat.RV22015.
5. Nogles TE, Galuska MA. Middle Cerebral Artery Stroke. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023.
6. Varkey BP, Joseph J, Varghese A, Sharma SK, Mathews E, Dhandapani M, et al. The distribution of lifestyle risk factors among patients with stroke in the Indian setting: systematic review and meta-analysis. Ann Neurosci. 2023;30(1):40-53. doi:10.1177/09727531221115899.
7. Sylaja PN, Pandian JD, Kaul S, Srivastava MVP, Khurana D, Schwamm LH, et al. Ischemic stroke profile, risk factors and outcomes in India: the Indo-US Collaborative Stroke Project. Stroke. 2018;49(1):219-222. doi:10.1161/STROKEAHA.117.018700.
8. Pandian JD, Sudhan P. Stroke epidemiology and stroke care services in India. J Stroke. 2013;15(3):128-134. doi:10.5853/jos.2013.15.3.128.
9. Lipska K, Sylaja PN, Sarma PS, Thankappan KR, Kutty VR, Vasan RS, et al. Risk factors for acute ischaemic stroke in young adults in South India. J Neurol Neurosurg Psychiatry. 2007;78(9):959-963. doi:10.1136/jnnp.2006.106831.
10. Moond V, Bansal K, Jain R. Risk factors and subtyping of ischemic stroke in young adults in the Indian population. Cureus. 2020;12(11):e11388. doi:10.7759/cureus.11388.
11. Pan B, Jin X, Jun L, Qiu S, Zheng Q, Pan M. The relationship between smoking and stroke: a meta-analysis.

Medicine (Baltimore). 2019;98(12):e14872. doi:10.1097/MD.0000000000014872.
12. Luo J, Tang X, Li F, Wen H, Wang L, Ge S, et al. Cigarette smoking and risk of different pathologic types of stroke: a systematic review and dose-response meta-analysis. Front Neurol. 2022;12:772373. doi:10.3389/fneur.2021.772373.
13. Bhat VM, Cole JW, Sorkin JD, Wozniak MA, Malarcher AM, Giles WH, et al. Dose-response relationship between cigarette smoking and risk of ischemic stroke in young women. Stroke. 2008;39(9):2439-2443. doi:10.1161/STROKEAHA.107.510073.
14. Li B, Li D, Liu JF, Wang L, Li BZ, Yan XJ, et al. Smoking paradox is not true in patients with ischemic stroke: a systematic review and meta-analysis. J Neurol. 2021;268(6):2042-2054. doi:10.1007/s00415-019-09596-3.
15. Kurmann R, Engelter ST, Michel P, Luft AR, Wegener S, Branscheidt M, et al. Impact of smoking on clinical outcome and recanalization after intravenous thrombolysis for stroke: a multicenter cohort study. Stroke. 2018;49(5):1170-1175. doi:10.1161/STROKEAHA.117.017976.
16. von Martial R, Gralla J, Mordasini P, El Koussy M, Bellwald S, Volbers B, et al. Impact of smoking on stroke outcome after endovascular treatment. PLoS One. 2018;13(5):e0194652. doi:10.1371/journal.pone.0194652.
17. Zhao Z, Zhao Z, Zheng X, Li X, Li X, Huang C, et al. The association between smoking and unfavorable outcomes in acute ischemic stroke patients with mechanical thrombectomy. Tob Induc Dis. 2020;18:31. doi:10.18332/tid/119229.
18. Wang HK, Huang CY, Sun YT, Li JY, Chen CH, Sun Y, et al. Smoking paradox in stroke survivors?: uncovering the truth by interpreting 2 sets of data. Stroke. 2020;51(4):1248-1256. doi:10.1161/STROKEAHA.119.027012.