



Cerebral Artery Stenosis Patterns in Ischemic Stroke Patients With and Without Opium Use

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Abstract

Introduction: Ischemic stroke is one of the most prevalent neurological disorders worldwide. Although several vascular risk factors have been identified for stroke, opium addiction has emerged as a potential contributing factor. This study aimed to compare the topography of cerebral arterial stenosis between opium-addicted and non-addicted patients with ischemic stroke.

Methods: This descriptive-analytical cross-sectional study was conducted on patients diagnosed with ischemic stroke. A total of 99 patients, including 25 opium-addicted and 74 non-addicted individuals, were enrolled. Demographic and clinical characteristics were collected for all participants. Duplex ultrasonography of the cerebral arteries was performed, and the severity and anatomical distribution of arterial stenosis were assessed and recorded.

Results: Assessment of arterial stenosis revealed that 65.7% of patients had normal arteries, 21.2% had stenosis of less than 70%, and 13.1% had stenosis greater than 70%. The most frequently affected vessels were the internal carotid artery (ICA) (18.2%) and the middle cerebral artery (MCA) (6.1%). Opium addiction was significantly more prevalent among male patients ($P=0.03$). Although the frequency of arterial stenosis was higher in opium-addicted patients compared to non-addicted patients, the difference was not statistically significant ($P=0.49$). Similarly, no significant difference was observed in the anatomical distribution of arterial stenosis between the two groups ($P=0.24$). Older age ($P=0.025$) and the presence of underlying cardiovascular disease ($P=0.01$) were significantly associated with greater arterial stenosis severity.

Conclusion: Although cerebral arterial stenosis was more frequently observed among opium-addicted patients than non-addicted patients, the difference did not reach statistical significance. Advanced age and underlying cardiovascular diseases were significantly associated with increased severity of cerebral arterial stenosis.

Keywords: Ischemic stroke, Opium addiction, Cerebral arteries, Arterial stenosis, Carotid stenosis, Duplex ultrasonography

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Introduction

Ischemic stroke is a leading cause of mortality and long-term disability worldwide, imposing a substantial burden on healthcare systems, particularly in low- and middle-income countries. In 2016, stroke was responsible for approximately 5.5 million deaths globally, nearly 80% of which occurred in developing countries.^{1,2} Iran is among the countries with a relatively high incidence of stroke, and its burden continues to increase due to the growing prevalence of vascular risk factors, including hypertension, diabetes mellitus, dyslipidemia, and smoking.^{3,4}

Although traditional vascular risk factors are well established in the pathogenesis of large-vessel atherosclerotic stroke, emerging evidence suggests that substance abuse, particularly opium addiction, may also contribute to

the development and progression of ischemic stroke.⁵⁻⁹ Opium, a natural substance derived from the poppy plant (*Papaver somniferum*), is widely used for both recreational and medicinal purposes in several regions of the world. In Iran, opium abuse represents a major public health and social challenge, with reported prevalence rates reaching 13.1% among adults in certain regions, including Kerman Province.¹⁰⁻¹² Opium contains several biologically active alkaloids, most notably morphine, which exert significant physiological effects and may lead to dependence as well as a range of adverse health outcomes.^{13,14} Indeed, opium and its derivatives are among the most commonly abused substances in the Iranian population.^{15,16} Given the high prevalence of opium use in Iran, particularly in Kerman, and its potential effects on vascular physiology, further



investigation into its impact on the cerebral vasculature is warranted.¹⁷ Several studies have reported a higher prevalence of opium addiction among patients with ischemic stroke compared with the general population.^{15,16} Experimental and clinical evidence suggests that opium use may adversely affect vascular function through multiple mechanisms, including acceleration of atherosclerosis, increased carotid intima-media thickness, endothelial dysfunction, and alterations in cerebral hemodynamics.¹⁷⁻²¹ Furthermore, neuroimaging studies have indicated that opium-addicted individuals may develop more extensive ischemic lesions than non-addicted patients.²²⁻²⁴ Despite these findings, the anatomical distribution and severity of cerebral arterial stenosis among opium-addicted patients with ischemic stroke remain insufficiently characterized. A better understanding of the relationship between opium addiction and cerebrovascular stenosis may improve risk stratification, diagnostic evaluation, and management strategies in this high-risk population.

Therefore, the present study aimed to compare the anatomical distribution (topography) and severity of cerebral arterial stenosis between opium-addicted and non-opium-addicted patients with ischemic stroke using duplex ultrasonography.

Materials and Methods

Study Design and Setting

This descriptive-analytical cross-sectional study was conducted at Shafa Hospital, a tertiary referral center in Kerman, Iran, in 2023.

Study Population

The study population consisted of adult patients admitted with a diagnosis of ischemic stroke. The diagnosis was established based on clinical evaluation and confirmed by brain magnetic resonance imaging (MRI). To exclude cardioembolic sources, all patients underwent comprehensive cardiac assessment, including electrocardiography (ECG), transthoracic echocardiography (TTE), and at least three days of continuous cardiac monitoring. In patients with suspected cardioembolic stroke, transesophageal echocardiography (TEE) was additionally performed. Patients with cardioembolic stroke, lacunar infarction, or other identified etiologies of stroke were excluded from the study.

Inclusion and Exclusion Criteria

Inclusion Criteria

Patients were eligible for inclusion if they met the following criteria:

- Age ≥ 18 years
- Confirmed diagnosis of ischemic stroke
- Underwent duplex ultrasonographic evaluation of cerebral arteries
- Provided written informed consent

Exclusion Criteria

Patients were excluded if they met any of the following criteria:

- Cardioembolic stroke confirmed by TEE or other diagnostic evaluations
- Lacunar infarction
- Presence of significant underlying diseases other than diabetes mellitus, hyperlipidemia, ischemic heart disease, or hypertension
- Use of medications unrelated to the treatment of diabetes mellitus, hyperlipidemia, ischemic heart disease, or hypertension
- Receipt of thrombolytic therapy before vascular assessment
- Inability to undergo duplex ultrasonography because of technical limitations, such as an inadequate acoustic window

Definition of Opium Addiction

Opium addiction was defined according to the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).²⁵ Based on clinical assessment and patient history, participants were categorized into either the opium-addicted or non-opium-addicted group.

Data Collection

Demographic and clinical information was collected using a standardized data collection form. Variables included age, sex, smoking status, history of hypertension, diabetes mellitus, hyperlipidemia, ischemic heart disease, and opium addiction.

Duplex Ultrasonographic Assessment

All participants underwent duplex ultrasonographic examination of the cerebral arteries. The following vessels were evaluated:

- Internal carotid artery (ICA)
- Common carotid artery (CCA)
- Middle cerebral artery (MCA)
- Anterior cerebral artery (ACA)
- Posterior cerebral artery (PCA)
- Vertebral artery (VA)
- Basilar artery (BA)

The severity of arterial stenosis was classified into three categories:

- No stenosis
- Stenosis $< 70\%$
- Stenosis $\geq 70\%$

In addition, the anatomical distribution (topography) of stenotic lesions was recorded for each patient.

Sample Size Calculation

The sample size was determined based on the data from a previous study.²⁶ Using G*Power software and assuming a statistical power of 95%, a minimum sample size of 99 participants was calculated. Accordingly, 99 patients were enrolled, including 25 opium-addicted and 74 non-opium-addicted individuals.

Ethical Considerations

The study protocol was approved by the Ethics

Committee of Kerman University of Medical Sciences (Ethical Code: IR.KMU.AH.REC.1402.013). Written informed consent was obtained from all participants or their legal representatives before enrollment. Participant confidentiality was maintained throughout the study, and no procedures beyond routine diagnostic evaluations were performed.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD), whereas categorical variables were reported as frequencies and percentages. Comparisons of continuous variables between groups were performed using the independent-samples t-test. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. A two-sided P value < 0.05 was considered statistically significant.

Results

A total of 99 patients with confirmed ischemic stroke were enrolled in the study, including 25 patients with a history of opium addiction and 74 patients without opium addiction. The mean age of the study population was 64.2 ± 9.5 years (range: 44–96 years). Overall, 57 patients (57.6%) were male, and 42 (42.4%) were female.

Baseline Characteristics

The demographic and clinical characteristics of the study participants are presented in Table 1. A significantly higher proportion of male patients was observed in the opium-addicted group compared to the non-opium-addicted group (80.0% vs. 50.0%, $P = 0.03$). No statistically significant differences were found between the two groups regarding mean age ($P = 0.18$), smoking status ($P = 0.28$), hypertension ($P = 0.62$), diabetes mellitus ($P = 0.82$), or ischemic heart disease ($P = 0.41$).

Overall, the two groups were comparable regarding most baseline demographic and clinical characteristics, except for sex distribution, which showed a significantly higher

proportion of males among opium-addicted patients.

Severity of Cerebral Arterial Stenosis

Arterial Stenosis Severity

Duplex ultrasonography showed that 65.7% of patients had no detectable arterial stenosis, 21.2% had stenosis $< 70\%$, and 13.1% had stenosis $\geq 70\%$.

Stenosis of any degree (i.e., $< 70\%$ or $\geq 70\%$) was more frequently observed among opium-addicted patients than among non-opium-addicted patients (44.0% vs. 31.1%). However, this difference was not statistically significant ($P = 0.49$).

Similarly, severe stenosis ($\geq 70\%$) was more prevalent in the opium-addicted group than in the non-opium-addicted group (16.0% vs. 12.2%), but the difference was not statistically significant ($P = 0.69$) (Table 2).

Topography and Distribution of Cerebral Arterial Stenosis

Among patients with ischemic stroke, the internal carotid artery (ICA) was the most frequently affected vessel, accounting for 18.2% of all stenotic lesions, followed by the middle cerebral artery (MCA) (6.1%). Concurrent involvement of both the ICA and MCA was observed in 7.1% of patients. Less frequently affected vessels included the vertebral artery (VA), posterior cerebral artery (PCA), and combinations of stenosis involving the VA, anterior cerebral artery (ACA), and ICA.

When classified according to vascular territory, the majority of stenotic lesions were located within the anterior circulation (91.2%), 5.9% were identified in the posterior circulation, and 2.9% involved both anterior and posterior circulations.

Comparison of the anatomical distribution of cerebral arterial stenosis between opium-addicted and non-opium-addicted patients revealed no statistically significant difference ($P = 0.24$) (Table 3).

Association Between Opium Addiction and Severity of Cerebral Arterial Stenosis

Based on duplex ultrasonographic findings, 65.7% of patients had no evidence of arterial stenosis, while 21.2% had stenosis of less than 70%, and 13.1% had stenosis of 70% or greater.

The overall prevalence of cerebral arterial stenosis was higher among opium-addicted patients than among non-opium-addicted patients (44.0% vs. 31.1%). However, this difference was not statistically significant ($P = 0.49$).

Likewise, severe stenosis ($\geq 70\%$) was more frequently

Table 1. Baseline characteristics of opium-addicted and non-opium-addicted patients

Characteristic	Opium Group (n=25)	Non-Opium Group (n=74)	P value
Male (%)	80%	50%	0.03
Mean Age (years)	62.4 $\pm$ 8.1	65.1 $\pm$ 10.2	0.18
Hypertension (%)	64%	58%	0.62
Diabetes (%)	36%	41%	0.82
Current Smoking (%)	48%	34%	0.28

Table 2. Comparison of the vascular stenosis severity based on patients' age

Severity of vascular stenosis	Mean age	SD of age	P value
Normal	62.80	9.29	
Less than 70%	64.81	7.97	0.025
More than 70%	70.54	10.93	

Table 3. Anatomical Distribution of Cerebral Arterial Stenosis by Opium Addiction Status

Vascular Territory	Opium-Addicted (n)	Percentage	Non-Addicted (n)	Percentage	P value
Anterior circulation	9	81.8%	22	95.7%	0.24
Posterior circulation	1	9.1%	1	4.3%	—
Both anterior-posterior	1	9.1%	0	0.0%	—

observed in the opium-addicted group compared to the non-opium-addicted group (16.0% vs. 12.2%). Nevertheless, the difference did not reach statistical significance ($P=0.69$) (Table 4).

Factors Associated with the Severity of Cerebral Arterial Stenosis

Analysis of factors associated with the severity of cerebral arterial stenosis demonstrated that older age was significantly associated with severe stenosis ($\geq 70\%$). Patients with severe stenosis had a higher mean age than those without severe stenosis (68.1 vs. 62.3 years, $P=0.025$).

In addition, the presence of underlying comorbidities, including hypertension, diabetes mellitus, and ischemic heart disease, was significantly associated with a higher frequency of arterial stenosis ($P=0.01$).

Although opium addiction was significantly more common among male patients ($P=0.03$), no significant association was observed between sex and the severity of cerebral arterial stenosis ($P=0.42$) (Table 5).

Distribution of Cerebral Arterial Stenosis According to Opium Addiction Status

The internal carotid artery (ICA) was the most frequently affected vessel, followed by the middle cerebral artery (MCA). Simultaneous involvement of multiple cerebral arteries was observed in a small proportion of patients. Comparison of the anatomical distribution of cerebral arterial stenosis between opium-addicted and non-opium-addicted patients revealed no statistically significant differences in the location of stenotic lesions ($P=0.24$) (Table 6).

Discussion

Ischemic stroke is one of the most prevalent neurological disorders worldwide and remains a major cause of mortality and long-term disability. Several established risk factors, including advanced age, hypertension, diabetes mellitus, dyslipidemia, smoking, and alcohol consumption, contribute to the development of ischemic stroke.^{27,28} In recent years, opium addiction has emerged as a potential risk factor for cerebrovascular disease. Previous studies

have reported a higher prevalence of opium addiction among patients with stroke than in the general population.²⁹ Furthermore, growing evidence suggests that opium may adversely affect vascular structure and function.^{30,31} Nevertheless, data regarding the anatomical distribution and severity of cerebrovascular stenosis in opium-addicted patients remain limited.

In the present study, we evaluated the pattern of cerebral arterial stenosis using duplex ultrasonography in 99 patients with ischemic stroke, including²⁵ opium-addicted and 74 non-opium-addicted individuals. Our findings demonstrated that arterial stenosis was more common among opium-addicted patients than among non-opium-addicted patients (44.0% vs. 31.1%). Similarly, severe stenosis ($\geq 70\%$) was observed more frequently in the opium-addicted group. However, neither difference reached statistical significance. In addition, no significant difference was found in the anatomical distribution of stenotic lesions between the two groups.

These findings are consistent with those reported by Hamzeh Moghadam et al, who found no significant differences in either the prevalence or anatomical distribution of cerebrovascular stenosis between opium-addicted and non-opium-addicted patients with ischemic stroke.²⁶ Similarly, Enhesari et al. reported no significant association between opium addiction and carotid intima-media thickness.³² Collectively, these findings suggest that although opium use may influence cerebrovascular health, its effect on the severity and anatomical distribution of arterial stenosis may be limited or difficult to detect in relatively small study populations.

Despite the absence of significant differences in stenosis severity and distribution, other studies have demonstrated important vascular effects of opium use. Moaddabi et al. reported significant alterations in cerebrovascular hemodynamic parameters among opium-addicted patients with ischemic stroke, showing a tenfold increased risk of abnormal pulsatility index (PI) and a threefold increased risk of abnormal mean flow velocity (MFV).²² Likewise, Mousavi et al. found that the number of atherosclerotic plaques was significantly higher in opium-addicted patients than in non-addicted individuals.²³

Additional evidence supports the association between opium use and adverse cerebrovascular outcomes. Iranmanesh et al. demonstrated that patients with

Table 4. Severity of Cerebral Arterial Stenosis by Opium Addiction Status

Stenosis Severity	Opium-Addicted (n)	Percentage (%)	Non-Addicted (n)	Percentage (%)	P value
No stenosis	14	56.0	51	68.9	0.49
Stenosis < 70%	7	28.0	14	18.9	—
Stenosis $\geq 70\%$	4	16.0	9	12.2	—

Table 5. Severity of Stenosis by Presence of Underlying Disease

Stenosis Severity	With Comorbidity (n)	Percentage (%)	Without Comorbidity (n)	Percentage (%)	P value
No stenosis	41	56.9	24	88.9	0.01
Stenosis < 70%	19	26.4	2	7.4	—
Stenosis $\geq 70\%$	12	16.7	1	3.7	—

Table 6. Anatomical Distribution of Vascular Stenosis Sites Among All Patients

Variable	Classification	F ¹	%
Artery of the vascular stenosis site	VA	1	1.0
	PCA	1	1.0
	MCA	6	6.1
	ICA	18	18.2
	MCA&ICA	7	7.1
	VA&ACA&ICA	1	1.0
	Total	34	34.3

F¹: Frequency

thrombotic stroke who were addicted to opium had significantly larger ischemic lesion volumes on magnetic resonance imaging (MRI) compared with non-addicted patients.²⁴ Furthermore, Hamzeh Moghadam et al. reported significantly greater carotid intima-media thickness among opium users.²¹ In a systematic review and meta-analysis, Mardi et al. have shown that opium abuse was associated with a 127% increase in the risk of stroke and a significantly higher risk of stroke-related mortality.³³ Taken together, these findings suggest that opium use may contribute to cerebrovascular pathology through mechanisms other than large-vessel stenosis alone, including alterations in vascular hemodynamics, endothelial function, and atherosclerotic burden.

Although the precise mechanisms underlying the association between opium use and cerebrovascular disease remain unclear, several biological pathways have been proposed. Previous studies have shown that opium consumption may increase plasma fibrinogen levels, promote systemic inflammation, accelerate atherosclerosis, and impair endothelial function.³⁴ Additionally, opium use has been associated with an increased risk of coronary artery disease and generalized atherosclerosis.^{35,36} Some investigations have also demonstrated unfavorable effects of opium on lipid metabolism, which may further contribute to the development of vascular disease.³⁷ These mechanisms may explain the increased burden of cerebrovascular complications observed among opium users despite the lack of significant differences in stenosis distribution in the present study.

Our findings also demonstrated that opium addiction was significantly more prevalent among male patients. Moreover, advanced age and the presence of underlying cardiovascular risk factors, including hypertension, diabetes mellitus, and ischemic heart disease, were significantly associated with greater severity of cerebral arterial stenosis. These results underscore the dominant role of traditional vascular risk factors in the pathogenesis of cerebrovascular stenosis and ischemic stroke.

The observed association between diabetes and vascular stenosis is supported by previous studies. Yang et al. demonstrated that diabetic patients are at increased risk of both carotid and intracranial arterial stenosis and are more likely to develop multiple cerebrovascular stenotic lesions.³⁸ Similarly, Goksan et al. reported that diabetes was associated with a 2.7-fold increased likelihood of high-grade carotid stenosis based on the findings of Doppler ultrasonography.³⁹ In addition, Suigimori et al. showed that hypertension is associated with significant alterations in cerebrovascular hemodynamics as assessed by transcranial Doppler ultrasonography.⁴⁰ These findings further emphasize the importance of controlling conventional cardiovascular risk factors in patients at risk of ischemic stroke.

Several limitations of this study should be acknowledged. First, the sample size of the opium-addicted group was relatively small, which may have reduced the statistical power to detect significant differences between the groups.

Second, assessment of vascular stenosis was solely based on duplex ultrasonography. The use of complementary vascular imaging modalities, such as computed tomography angiography (CTA) or magnetic resonance angiography (MRA), may provide more comprehensive and accurate characterization of cerebrovascular stenosis.

In conclusion, cerebral arterial stenosis was more frequently observed among opium-addicted patients with ischemic stroke than among non-opium-addicted patients; however, the difference was not statistically significant. Furthermore, advanced age and underlying cardiovascular comorbidities were significantly associated with greater stenosis severity. These findings suggest that while opium use may contribute to the overall cerebrovascular risk profile, traditional vascular risk factors remain the primary determinants of the severity of cerebral arterial stenosis in patients with ischemic stroke.

Conclusion

This cross-sectional study demonstrated that although cerebrovascular stenosis was more frequently observed among ischemic stroke patients with opium addiction than among non-addicted patients, the difference was not statistically significant. In contrast, advanced age and underlying cardiovascular comorbidities, particularly hypertension and diabetes mellitus, were significantly associated with greater stenosis severity.

These findings suggest that traditional vascular risk factors remain the primary determinants of cerebrovascular stenosis severity in patients with ischemic stroke. Although opium use may contribute to the overall cerebrovascular risk profile, its independent association with the anatomical distribution and severity of cerebral arterial stenosis remains uncertain. Future large-scale prospective studies incorporating advanced vascular imaging modalities are warranted to further elucidate the potential impact of opium use on cerebrovascular structural and functional abnormalities.

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Competing Interests

The authors declare that they have no conflict of interest.

Consent for Publication

Not applicable.

Data Availability Statement

Not applicable.

Ethical Approval

The study protocol was approved by the Ethics Committee of Kerman University of Medical Sciences (Ethical code: IR.KMU.AH.REC.1402.013).

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