ORIGINAL ARTICLE

Sonographic features of internal carotid artery in patients with opioid use disorder: Is opium a new risk factor for atherosclerosis of internal carotid artery?

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Background: Opium use disorder (OUD) is prevalent worldwide. Despite its traditional use, recent studies suggest that OUD may exacerbate atherosclerosis and ischemic stroke. This study investigates the effect of OUD on internal carotid artery sonographic findings using B-mode Doppler sonography. **Materials and Methods:** A case–control study was conducted in Isfahan, Iran, from 2021 to 2023. A total of 295 patients, including 95 with OUD and 200 without, were evaluated through medical records and B-mode Doppler sonography to assess atherosclerotic plaques, vulnerability of plaques, carotid artery stenosis, and carotid artery intima–media thickness (CIMT). Data on age, sex, smoking, and medical history were also collected. **Results:** The OUD group had a higher prevalence of tobacco smoking (56% vs. 18%; $P < 0.001$). Atherosclerotic plaques were more common in OUD patients (83% vs. 65%; $P = 0.001$). Vulnerable plaques were more frequent in OUD patients (19% vs. 9%; $P = 0.039$). OUD patients were three times more likely to have carotid artery stenosis (85% vs. 65%; $P < 0.001$) and had a higher incidence of more than 70% stenosis (33.8% vs. 16%; $P = 0.003$). CIMT was significantly higher in the OUD group (0.95 mm vs. 0.87 mm; $P < 0.001$). Logistic regression analysis revealed that OUD was independently associated with atherosclerotic plaque, carotid stenosis, stenosis of more than 70%, and CIMT ($P < 0.05$). **Conclusion:** This study highlights a significant association between OUD and sonographic markers of carotid atherosclerosis, including increased intima–media thickness, higher prevalence of atherosclerotic plaques, and stenosis of more than 70%. We suggest OUD as a potential risk factor for carotid artery atherosclerosis.

Key words: Atherosclerosis, atherosclerotic plaque, internal carotid artery, intima-media thickness, opium

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INTRODUCTION

Opium has been traditionally used for medicinal and recreational purposes and is the second-most widely consumed illicit drug globally after cannabis.[1] In 2017, the United Nations Office on Drugs and Crime reported that 29 million people had used opiates in the preceding year, which is 50% higher than previous estimates.[2] In the Middle East, particularly in Iran, opium remains the most commonly abused substance after tobacco.[3]

There is a traditional belief that opium may have beneficial effects on cardiovascular diseases (CVDs), diabetes mellitus (DM), hypertension (HTN), and dyslipidemia (DLP).[4] This belief has significantly shaped public perceptions and may lead to biases in health-seeking behavior, as well as underestimation of the potential harms of opium use. Such perceptions can contribute to delayed diagnosis and management of opium-related complications, including its impact on atherosclerosis and ischemic stroke. Previous studies have evaluated the effect of opium on ischemic

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stroke, and a systematic review conducted in 2022 found that opium use disorder increases both the incidence and mortality of ischemic stroke.[5] Atherosclerosis is one of the most critical mechanisms of ischemic stroke. HTN, DLP, DM, and cigarette smoking are well-known risk factors for atherosclerosis. Recent studies have also suggested that opium addiction could be considered a risk factor for atherosclerosis;[6] however, the role of opioid use disorder (OUD) as a risk factor for CVDs, particularly atherosclerosis, remains underexplored. B-mode Doppler sonography is a sensitive and accurate tool for evaluating the characteristics of cervical arteries.[7] This study aims to investigate the effect of opioid use disorder (OUD) on the sonographic findings of the internal carotid artery (ICA) using B-mode Doppler sonography.

MATERIALS AND METHODS

This case–control study was conducted in Isfahan, Iran; from 2021 to 2023 by reviewing existing medical records and files in the medical documents and records department of Al-Zahra Hospital. After obtaining informed consent from the participants, 295 patients who underwent B-mode Doppler sonography were enrolled; 95 patients had OUD, and 200 did not. OUD is defined as the chronic use of opioids causing clinically significant distress or impairment.[8] Patients with a history of other substance abuse and a history of ICA stenting were excluded from the study.

The data collected from patients included age, sex, tobacco smoking, blood pressure, history of ischemic stroke, history of HTN, history of DM, history of DLP, and sonographic parameters of carotid arteries. Hypertensive patients were defined as those with either a history of HTN or high blood pressure upon admission (systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg).

Participants underwent bilateral carotid Doppler ultrasound using an S6GE ultrasound machine to evaluate atherosclerotic plaques, arterial stenosis, and measure carotid intima-media thickness (CIMT). Atherosclerotic plaques were categorized into vulnerable and nonvulnerable types. Uniformly echolucent plaques (type 1) and predominantly echolucent plaques (type 2) were defined as vulnerable. Predominantly echogenic plaques (type 3), uniformly echogenic plaques (type 4), and plaques with heavy calcification (type 5) were defined as nonvulnerable.[9] Carotid stenosis was classified as below 70% and above 70%. Intima–media thickness was measured using a high-resolution B-mode ultrasound scanner, assessing the thickest point of the carotid intima–media in the common carotid artery, carotid bulb, and ICA on both sides. The intima–media thickness was defined as the distance between the intima–lumen edge and the adventitia–intima edge. The mean intima–media thickness for both sides was considered. To minimize bias, the sonographers performing the Doppler ultrasound examinations were blinded to the participants' opioid use disorder (OUD) status.

Statistical analysis

The collected data were entered into SPSS v 22.0 software (IBM Corporation, Armonk, NY, USA). Descriptive statistical indices such as mean, standard deviation (SD), frequency, and percentage were used to describe the data. Quantitative results are presented as mean ± SD. Independent *t*-tests, Chi-square tests, and if necessary, Fisher's exact test were used for data analysis. Logistic regression was performed to evaluate the effects of opioid use disorder on the likelihood of patients having atherosclerotic plaques, carotid stenosis, vulnerable plaques, and CIMT.

RESULTS

In this study, 295 patients (98 female and 197 male) were surveyed. Among them, 95 had OUD, and 200 did not. Table 1 shows the demographic and clinical characteristics of both groups. The mean age of patients was 67.41 years (SD = 10.06) in the OUD group and 66.53 years (SD = 13.32) in the non-OUD group (P = 0.56). Tobacco smoking was more prevalent in patients with OUD (56% vs. 18%; P < 0.001, 95% confidence interval [CI] =3.48–10.32). There were no significant differences in terms of HTN, DM, and DLP between the OUD and non-OUD patients (P > 0.05).

The atherosclerotic plaque was more prevalent among patients with OUD (83% vs. 65%; P = 0.001, 95% CI = 1.44–4.89). Comparison of plaque types in terms of vulnerability showed statistically significant differences between the two groups (19% vs. 9%; P = 0.039, 95% CI = 0.19–1). Patients with OUD were three times more likely to have carotid artery stenosis than non-OUD patients (85% vs. 65%; P < 0.001, 95% CI = 1.59–5.69). Carotid stenosis of more than 70% was more prevalent among patients with OUD (33.8% vs. 16%; P = 0.003, 95% CI = 1.38–5.15). CIMT was 0.95 mm (SD = 0.15) in OUD patients and 0.87 mm (SD = 0.17) in non-OUD patients, showing statistically significant differences between the two groups (P < 0.001).

The logistic regression model used to evaluate the independent effect of OUD on sonographic features of the carotid artery showed that patients with OUD were more likely to have atherosclerotic plaque, carotid stenosis, and stenosis of more than 70% (P < 0.05) [Table 2].

DISCUSSION

Known risk factors for atherosclerosis include HTN, DM, smoking, and DLP. Recent studies have shown a higher

Table 1: Comparing demographic and sonographic characteristics of the cervical carotid artery in opioid use disorder and nonopioid use disorder groups

Variable	Group		*P*	OR (95% CI)
	OUD (*n*=95), *n* (%)	Non-OUD (*n*=200), *n* (%)		
Age (years), mean±SD	67.41±10.06	66.53±13.32	0.56	N/A
Sex				
Male	89 (93.7)	108 (54.0)	<0.001*	12.63 (5.28–30.22)
Female	6 (6.3)	92 (46.0)		
Tobacco smoking	54 (56.8)	36 (18.0)	<0.001*	6 (3.48–10.32)
HTN	54 (56.8)	126 (63.0)	0.37	0.77 (0.47–1.27)
DM	57 (60)	125 (62.5)	0.70	1.11 (0.67–1.83)
Hyperlipidemia	45 (31)	100 (69)	0.70	0.90 (0.55–1.46)
Atherosclerotic plaque	79 (83.2)	130 (65)	0.001*	2.65 (1.44–4.89)
Plaque types				
Vulnerable	15 (19)	12 (9.4)	0.039*	0.44 (0.19–1)
Nonvulnerable	64 (81)	116 (90.6)		
Carotid artery stenosis	80 (85.1)	131 (65)	<0.001*	3.01 (1.59–5.69)
Carotid stenosis degree (%)				
<70	53 (66.3)	110 (84)	0.003*	2.66 (1.38–5.15)
>70	27 (33.8)	21 (16)		
CIMT (mm)	0.95±0.15	0.87±0.17	<0.001*	N/A

*Statistically significant differences. CIMT=Carotid artery intima–media thickness; OUD=Opioid use disorder; SD=Standard deviation; N/A=Not applicable, CI=Confidence interval, OR=Odds ratio, DM=Diabetes mellitus, HTN=Hypertension

Table 2: Logistic regression subgroup analysis of opium use disorder on sonographic findings of carotid artery independence of age, tobacco smoking, hypertension, diabetes mellitus, and dyslipidemia

Dependent variable	*P*
Atherosclerotic plaque	0.002*
Plaque types	0.070
Carotid artery stenosis	0.002*
Carotid stenosis degree	0.001*
CIMT (mm)	0.001*

*Statistically significant differences. CIMT=Carotid artery intima–media thickness

prevalence of cardiovascular disorders in patients with opium addiction,[10] highlighting the negative impact of opium on the cardiovascular and cerebrovascular system.[11-14] Given the similarity in atherosclerosis pathobiology in the heart and brain and the significant role of carotid atherosclerosis in ischemic stroke occurrence, assessing new risk factors for carotid artery atherosclerosis is crucial. This study focused on the sonographic features of the carotid artery in patients with opium use disorder (OUD) compared to those without. ICA plaques, carotid stenosis, and CIMT are indicators of atherosclerosis. Increased CIMT is a strong predictor of cardiovascular events. Calcification of plaques indicates stability, reducing the likelihood of thromboembolism, whereas vulnerable plaques with fibrous caps have a higher risk of rupture and subsequent embolization, causing stroke.[15,16] Our study found that OUD is associated with more frequent atherosclerotic plaques, vulnerable plaques, carotid artery stenosis, stenosis of more than 70%, and increased CIMT. After excluding age, HTN, DM, smoking, and DLP, significant differences remained between patients with and without OUD regarding these sonographic findings. This indicates a higher susceptibility to atherosclerosis and a higher risk of vulnerable plaque formation in the ICA among OUD patients, suggesting a potential for subsequent embolization.

Previous studies evaluating the effect of opium on carotid artery atherosclerosis are limited.[7,17,18] Hamzei-Moghaddam *et al*. evaluated 97 patients with ischemic stroke and found no statistically significant difference in stenosis and stenosis location among patients with and without opium addiction who presented with ischemic stroke, although only three patients had ICA stenosis in this study.[7] Enhesari *et al*. found no significant relationship between opium addiction and CIMT, potentially due to the younger age of participants in their study (mean age of participants was 42.28 ± 12.58 in the addicted group and 35.99 ± 15.38 in the nonaddicted group).[18] Moreover, age is a significant known factor for atherosclerosis of the ICA artery and the differences in terms of age between addicted and nonaddicted patients in the Enhesari *et al*. study showed a significant difference (P = 0.001). These findings cast doubt on the ability of the aforementioned studies to detect significant differences. Shirani *et al*. found no significant differences in carotid stenosis of more than 70% between patients with and without OUD, although they did not evaluate other sonographic findings.[17]

Atherosclerosis formation involves complex mechanisms, including endothelial dysfunction, oxidative stress, and chronic inflammation, leading to plaque formation in arterial walls. Angiotensin II generates reactive oxygen

species, which oxidize low-density lipoprotein, promoting inflammatory and atherogenic activities. Smooth muscle cells migrate and proliferate in the intima layer, transforming into foam cells that drive plaque buildup.[16] Opium use exacerbates these processes by increasing oxidative stress and inflammation, accelerating endothelial dysfunction and plaque progression. Furthermore, opium is associated with elevated homocysteine, plasma fibrinogen, and plasminogen activator inhibitor-1, which heighten the risk of atherosclerosis. Impurities like lead in opium and lifestyle factors such as reduced physical activity also contribute to cardiovascular risks.[6,10]

While our study provides compelling evidence of a link between OUD and carotid atherosclerosis in an Iranian cohort, the pathophysiological mechanisms and the control for traditional risk factors suggest that these findings may have broader applicability. These findings highlight the need for increased awareness, targeted screening, and comprehensive management strategies to address the cardiovascular and cerebrovascular risks associated with OUD. However, several limitations warrant consideration; the case–control design limits causal inferences, and the single-center setting may restrict the generalizability of the results. Future research should aim to validate our results in broader populations, establish causality, and explore the feasibility of integrating atherosclerosis screening into addiction treatment programs.

CONCLUSION

We observed that individuals with opium use disorder had a higher prevalence of ICA plaques and carotid stenosis. Their plaques were more vulnerable, significant carotid stenosis was more common, and CIMT was greater in these patients. According to our findings, we suggest opioid use disorder as a potential risk factor for atherosclerosis.

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Conflicts of interest

There are no conflicts of interest.

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