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Original Research Article

Is opium use a predictor factor for major adverse cardiovascular events in coronary angiography patients?

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Abstract

Objective: It is believed that opium, as a narcotic substance, may have protective effects against various disorders such as cardiovascular diseases. The association between opium use and the occurrence of major adverse cardiovascular events (MACE) in patients undergoing angiography was assessed in this study.

Materials and Methods: The present descriptive-analytical study was conducted on patients with suspected coronary artery disease (CAD) who underwent angiography at Razi Hospital, Birjand, Iran from June 2018 to November 2020. Participants were considered into two groups: Addicted (i.e. opium users) and non-opium users. Demographic information, medical history, history of opium use, and the SYNTAX score were collected.

Results: A total of 2,759 individuals with a mean age of 60.12 ± 18.12 years (ranging from 18 to 94 years) were included. Among the participants, 59.4% were male, with 627 identified as opium users and 2,132 as non-users. The opium user group exhibited significantly lower body mass index (BMI), and frequency of diabetes mellitus and hypertension compared to the non-opium user group ($p<0.001$). Conversely, the incidence of stenosis ≥50%, moderate SYNTAX score, and MACE incidence were remarkably higher among opium users compared to non-users ($p<0.01$ to $p<0.001$). Logistic regression analyses indicated a significant relationship between age, SYNTAX score, prior percutaneous coronary intervention (PCI), and opium use with cardiovascular procedures.

Conclusion: These results indicate that opium use is associated with increased stenosis and SYNTAX score, as well as a higher incidence of myocardial infarction and PCI, thereby increasing the odds ratio for cardiovascular events.

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Introduction

Cardiovascular diseases (CVDs) are the predominant causes of mortality worldwide, with coronary artery disease (CAD) being one of the most critical forms of these conditions. CAD stands as the principal cause of death in developed and developing countries (Alinejad et al. 2018; Eijsvogels et al. 2020). In 2016, the average total cost per patient was over $1881.4 and the total costs resulted in 1159.62 $million approximately 6.7% of the Iran gross domestic product (GDP), primarily due to CAD, imposed on the Iranian health system (Emamgholipour et al. 2018). A total of almost 18 million CAD deaths occur worldwide each year, and about 2 out of every 10 deaths are caused by this disease (Huxley et al. 2015).

Opium, a substance extracted from *Papaver somniferum*, is used traditionally for treating pain, diabetes, diarrhea, cough, and insomnia. It is supposed that the consumption of opium has useful effects on health, particularly atherosclerotic CVD risk factors including lipid profile, hypertension, and dyslipidemia in Eastern people (Martínez and Ballesteros 2019a).

In traditional Greek and Egyptian medicine, opium was utilized for its sedative properties to induce sleep and relieve pain. The medicinal applications of poppy plants extended to the treatment of various conditions including breast abscesses, agitation in infants, and as components in eye drops and topical ointments (Rosso 2010). Additionally, it has been suggested that opium was traditionally used to address diarrhea, dysentery, fevers, asthma, chronic cough, phthisis, and diabetes, functioning as a broad-spectrum analgesic (Martínez and Ballesteros 2019b). In Unani literature, opium is described as an analgesic, sedative, stimulant, and nutritive agent. It is reported to be beneficial in managing headaches, insomnia, cough, and biliary colic (Jafri et al. 2018).

The results of a study indicated an association between long-term opiate administration and a reduced incidence of myocardial infarction as well as decreased severity of CAD (Marmor et al. 2004). Additionally, hospital mortality rates and the occurrence of anterior wall myocardial infarction were significantly lower in opium users compared to non-users (Dehghani et al. 2013).

After tobacco, opium is the second most commonly used narcotic in the Middle East, with an estimated 2.3% of the adult population in Iran classified as opium addicts (Alinejad et al. 2018). While some studies suggest that opium use may mitigate certain CAD risk factors (Najafipour et al. 2021), it can lead to adverse effects through various mechanisms including alterations in coagulation, oxidative stress, increased inflammation, reduced physical actions, and adverse metabolic and hormonal changes (Hedayati-Moghadam et al. 2022). Consequently, conflicting results exist regarding the effects of opium on potential risk factors such as hypertension, lipid profiles, and diabetes.

Although the impact of opium use on CAD potent risk factors such as hypertension, plasma lipid levels, diabetes, and depression has been evaluated in several studies, few investigations have specifically addressed patients undergoing elective percutaneous coronary intervention (PCI). One study found that opium users undergoing PCI experienced higher rates of major adverse cardiovascular events (MACE) and mortality over a five-year period (Masoudkabir et al. 2020), while another study indicated that opium users had increased readmission rates (Safaei 2008).

Considering the high incidence of opium use in Iran, it is essential to accurately determine the correlation between opium use and MACE in PCI patients. Therefore, we aimed to assess the relationship between opium use and the

occurrence of MACE during the follow-up of patients undergoing angiography.

Materials and Methods

Participants

In this descriptive-analytical study, data were collected from all patients undergoing angiography at Razi Hospital, south Khorasan province, Birjand, Iran, between June 2018 and November 2020. Information was sourced from the Persian Registry of CVD (PROVE)(Khosravi et al. 2021), which serves as a local demonstration project for various types of CVD. This multi-center registry has been operational since March 2017.

All patients admitted to the hospital and undergoing angiography were involved in the study. The patients were excluded if their data related to MACE were unavailable or if follow-up was not possible due to reasons such as incorrect contact information or inactive mobile phones.

Demographic information (gender and age), comorbidities (including diabetes, hypertension, dyslipidemia, smoking, opium use, and overweight/obesity), and angiographic details including the SYNTAX score were collected. Patients who had never consumed opium were categorized as non-users, while those who reported consuming opium (at least one day a week) for a minimum of six months prior to admission, were classified as opium users. The methods of opium administration included both oral and inhalational routes, with oral use (59.1%) being the most common method of administration (Moezi et al. 2022).

The SYNTAX score serves as a valuable instrument for evaluating outcomes related to PCI in patients with multi-vessel CAD. An elevated SYNTAX score is associated with poorer prognoses and poses greater treatment challenge (Ozdemir 2020). Patients are categorized into risk categories based on their SYNTAX scores: low (<10), intermediate (11-20), and high risk (>20) (Magro et al. 2011). The SYNTAX score evaluates the coronary vasculature by considering the number of lesions, their functional significance, anatomical location, and overall complexity (Sianos et al. 2005).

Clinical follow-up

Following the acquisition of ethics approval from the Institutional Ethics Committee (IR.BUMS.REC.1401.437), patients were followed by phone, and a researcher-made checklist, including patients' death, hospitalization after angiography, and discharge, was completed. The exact causes of death (cardiac or non-cardiac) and hospitalization (cardiac or non-cardiac) were checked and confirmed by the event committee. The information on several patients could not be obtained due to incorrect contact numbers, so blocked numbers were excluded from the study. Patients in the 2 groups of opium and non-opium users were compared.

Study outcomes

The prime outcome of the study is the rate of MACE, which is defined as a composite endpoint encompassing all-cause mortality (both cardiac and non-cardiac), stroke, myocardial infarction, coronary revascularization (including PCI and coronary artery bypass grafting (CABG), and instances of hospitalization. To avoid overcomplicating the graph and to improve readability, only subgroups of demographic and clinical variables with a "present" or "positive" status (including hypertension, diabetes, dyslipidemia, family history of heart disease, smoking, overweight/obesity, and history of MI, PCI, or CABG) are included.

Statistical analysis

Statistical analyses were performed utilizing SPSS for Windows version 22.0 (SPSS Inc., Chicago, IL, USA). The normality of the data was evaluated using the Kolmogorov-Smirnov test. Continuous variables are reported as median (Q1-Q3), while categorical variables are presented as

frequency (%). Comparisons between unpaired samples were made using either the Student's t-test or the Mann-Whitney U test. Independent factors associated with MACE were identified through both univariate and multivariate logistic regression analyses. The results of both the univariate and multivariate regression analyses are expressed as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was established at a two-sided p-value of <0.05.

Results

Of 3370 coronary angiography patients, 2759 responded to telephone follow-up and were examined (Figure 1). The mean age of the participants was 60.12±18.12 years (age range 18-94 years), and they were mostly male (59.4%). CAD severity was categorized as non-obstructive or stenosis <50% (44%) and obstructive or stenosis ≥ 50% (56%). Risk factors in these individuals were in the following order of frequency: overweight and obesity (50.2%), hypertension (49%), dyslipidemia (27.3%), diabetes (25.8%), opium use (22.7%), and smoking (12.2%).

Baseline characteristics and comorbidities of opium and non-opium users were compared. The frequencies of male gender and smoking were significantly higher in the opium user than in the non-opium user group (p<0.001). The frequency of smoking was remarkably higher in the opium-user group; however, the BMI and the frequencies of diabetes and hypertension were higher in the non-opium user than in the opium-user group (p<0.001 for all).

The coronary stenosis ≥50%, SYNTAX score, and cardiovascular events such as myocardial infarction (MI) and PCI, were remarkably higher in the opium-user than in the non-opium user group (p<0.01 to p<0.001) (Table 1). The comparison of the frequency of MACE according to opium use and non-opium use is shown in Figure 2.

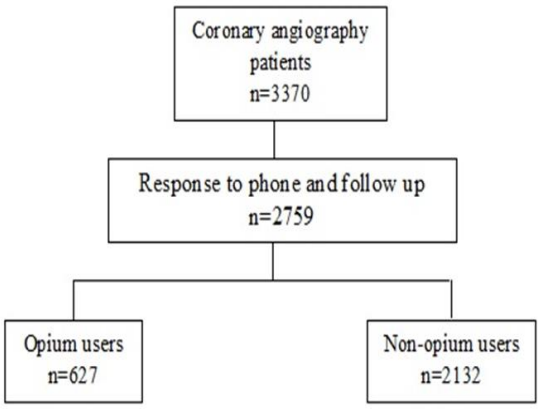

Figure 1. Flowchart of the selection of patients

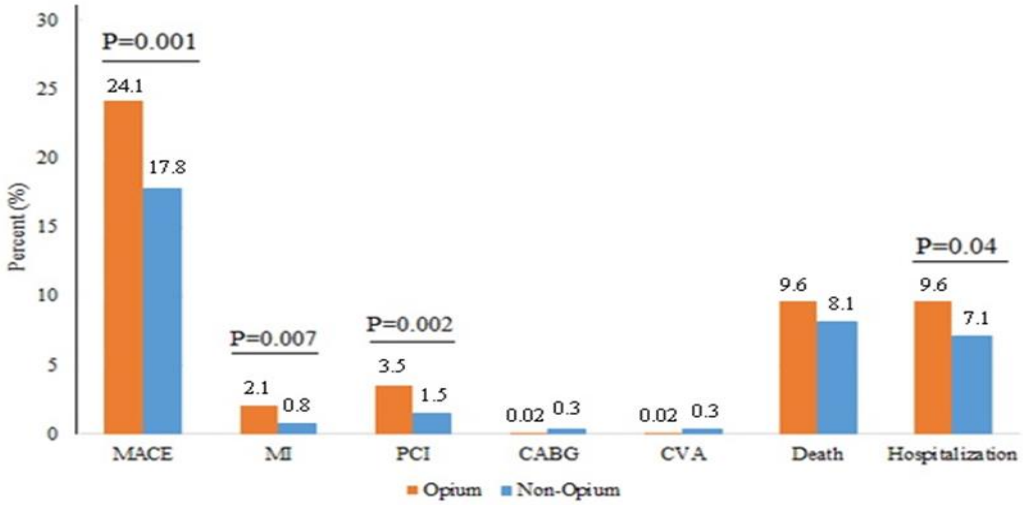

Figure 2. The frequency of major adverse cardiovascular events according to opium use and non-opium use. MACE: Major adverse cardiac event, MI: Myocardial infarction, CABG: Coronary artery bypass graft, PCI: Percutaneous coronary intervention, CVA: Cerebrovascular accident.

The mean follow-up period was 2.6 years (about 1 to 5 years). In the 1- to 5-year clinical follow-up, the incidence of total MACE was 19.2%, which was remarkably higher in the opium-user than in the non-opium user group (p<0.001). The causes of death were (8.8%) not significant between the two groups, but the frequencies of MI and PCI (1.1% and 1.9%, respectively) were remarkably higher in the opium-user group (Table 1).

We found that 25% of deaths occurred at home. The cause of 48% was cardiac, 60% non-cardiac, and 20% unknown. The incidence of PCI was statistically higher in the opium group, but there was no statistically remarkable difference in death, stroke, and CABG between the two groups.

The present study results showed a remarkable association between opium use and the severity of coronary artery involvement (the SYNTAX score). Univariate logistic regression analysis showed that age (OR: 1.03, 95% CI: 1.02-1.04), diabetes (OR: 1.33, 95% CI: 1.02-1.04), hypertension (OR: 1.45, 95% CI: 1.14-1.78), prior PCI (OR: 1.82, 95% CI: 1.33-2.4), opium use (OR: 1.32, 95% CI: 1.03-1.68,), SYNTAX score (OR: 1.03, 95% CI: 1.02-1.04) and number of affected vessels were remarkably correlated with MACE (Table 2).

Table 1. Demographic and clinical characteristics of the study participants

Variables		Opium user (n=627)	Non-Opium user (n=2132)	All (n=2759)	p-value
Age (Year)		60 [52-68]	61 [53-70]	61 [53-70]	0.063
Sex	Male	463(73.8)	1177 (55.2)	1640 (59.4)	<0.001
	Female	164 (26.2)	955 (44.8)	1119 (40.6)	
BMI					
Underweight		81(14.6)	95(4.9)	176 (7.1)	
Normal		248(44.8)	812(42.2)	1060 (42.8)	<0.001
Over weight		173(31.3)	696 (36.2)	869 (35.1)	
Obese		51(9.2)	322(16.7)	373 (15.1)	
Smoke	No	409 (67.7)	1921 (93.2)	2330 (87.4)	0.001
	Yes	195 (32.3)	141 (6.8)	336 (12.6)	
FH	No	504 (83.3)	1649 (80.2)	2153 (80.9)	0.084
	Yes	101 (16.7)	408 (19.8)	509 (19.1)	
DM	No	483 (80.8)	1490 (72.3)	1973 (74.2)	0.001
	Yes	115 (19.2)	570 (27.7)	685 (25.8)	
DLP	No	455 (75.6)	1474 (71.9)	1929 (72.7)	0.072
	Yes	147 (24.4)	577 (28.1)	724 (27.3)	
HTN	No	355 (59.2)	1001 (48.6)	1356 (51)	<0.001
	Yes	245 (40.8)	1058 (51.4)	1303 (49)	
Prior MI	No	543 (89.8)	1874 (91.2)	2417 (90.9)	0.265
	Yes	62 (10.2)	180 (8.8)	242 (9.1)	
Prior PCI	No	531 (87.6)	1857 (90.2)	2388 (89.6)	0.064
	Yes	75(12.4)	201 (9.8)	276 (10.4)	
Prior CABG	No	585 (96.4)	1996 (96.8)	2581 (96.7)	0.566
	Yes	22 (3.6)	65 (3.2)	87 (3.3)	
Stenosis ≥50%		440 (73.1)	1295 (63.9)	1635 (56)	0.001
Syntax					
Normal		62 (11.1)	216 (11.4)	278 (11.3)	
Low risk		240 (43)	932 (49.3)	1172 (47.8)	0.01
Intermediate		168 (30.1)	461 (24.4)	629 (25.7)	
High risk		88 (15.8)	283 (15)	371 (15.1)	
MACE	No	476 (75.9)	1752 (82.2)	2228 (80.8)	0.001
	Yes	151(24.1)	380(17.8)	531 (19.2)	
Hospitalization		60 (9.6)	152 (7.1)	212 (7.7)	0.044
MI		13(2.1)	16(0.8)	29 (1.1)	0.007
PCI		22(3.5)	31(1.5)	53 (1.9)	0.002
CABG		1 (0.2)	7(0.3)	8 (0.3)	0.692
CVA		1 (0.2)	6(0.3)	7 (0.3)	0.99
Death		60 (9.6)	182 (8.1)	242 (8.8)	0.44

Statistical tests: Chi-squared test or Fisher's exact test for categorical variables; Mann–Whitney U test for continuous variables. BMI: Body Mass Index, FH: Family history of CAD, DM: Diabetes mellitus, DLP: Dyslipidemia, HTN: Hypertension, MI: Myocardial infarction, CABG: Coronary artery Bypass Graft, PCI: Percutaneous Coronary Intervention, MACE: Major Adverse Cardiac Event (Death, Stroke, MI, PCI, CABG), CVA: Cerebrovascular accident.

Table 2. Univariate logistic regression analysis of MACE in patients

Variables	Univariate Logistic Regression	
	OR (95% CI)	**p-value**
Age (Year)	1.03(1.02-1.04)	0.001<
Sex (Male)	1.26(0.96-1.53)	0.05
BMI (kg/m2)	0.98(0.63-2.65)	0.08
Syntax	1.03(1.02-1.04)	0.001<
DM	1.33(1.02-1.04)	0.02
DLP	1.15(0.9-1.45)	0.25
HTN	1.45(1.14-1.78)	0.001<
FH	1.01(0.77-1.35)	0.93
Prior CABG	1.27(0.85-2.26)	0.35
Prior PCI	1.82(1.33-2.4)	0.001<
Opium & smoker	)2.35-0.89(1.22	0.29
Smoke	1.22(0.92-1.61)	0.164
Opium	)1.03-1.68(1.32	0.03

BMI: Body Mass Index, FH: Family history of CAD, DM: Diabetes mellitus, DLP: Dyslipidemia, HTN: Hypertension, CABG: Coronary artery Bypass Graft, PCI: Percutaneous Coronary Intervention.

Multivariate regression analysis also showed that prior PCI (OR: 1.92, 95% CI: 2.8 -1.21), opium use (OR: 1.5, 95% CI: 2.31 -1.05), diabetes (OR: 1.39, 95% CI: 1.86 -1.09), age (OR: 1.03, 95% CI: 1.01-1.04), and SYNTAX score (OR: 1.02, 95% CI: 1.01-1.03) were the independent risk factors for MACE (Table 3).

The relation between risk factors and the occurrence of MACE according to opium use is shown in Table 4.

Table 3. Multiple logistic regression analysis of MACE in patients

	Multiple Logistic Regression	
Variables	**OR (95% CI)**	**p-value**
Age (Year)	1.03(1.01-1.04)	<0.001
Syntax	1.02(1.01-1.03)	<0.001
DM	1.39(1.09 -1.86)	0.02
Prior PCI	1.92(1.21 -2.8)	<0.001
Opium	1.5(1.05 -2.31)	0.02

DM: Diabetes mellitus, PCI: Percutaneous Coronary Intervention

Table 4. The association between risk factors and the occurrence of major adverse cardiovascular events (MACE) according to opium use.

variable		MACE -Non Opium N (%)	MACE - Opium	p-value
sex	Male	222 (58.4)	106 (70.2)	0.007
	Female	158 (41.6)	45 (29.8)	
hypertension	No	148 (41)	77 (54.2)	0.005
	Yes	213 (59)	65 (45.8)	
Diabetes	No	247 (68.2)	102 (71.8)	0.24
	Yes	115 (31.8)	40 (28.2)	
dyslipidemia	No	251 (69.9)	105 (73.9)	0.21
	Yes	108 (30.1)	37 (26.1)	
Family history	No	297 (82.7)	118 (82.5)	0.52
	Yes	62 (17.3)	25 (17.5)	
Smoke	No	338 (93.6)	94 (65.3)	<0.001
	Yes	23 (6.4)	50 (34.7)	
BMI	Low	19 (5.9)	23 (18)	<0.001
	Normal	145 (45)	58 (45.3)	
	Overweight & obese	158 (49.1)	47 (36.7)	
Prior MI	No	312 (86.4)	119 (83.2)	0.21
	Yes	49 (13.6)	24 (16.8)	
Prior PCI	No	306 (84.8)	115 (79.9)	0.11
	Yes	55 (15.2)	29 (20.1)	
Prior CABG	No	344 (95.3)	137 (95.1)	0.55
	Yes	17 (4.7)	7 (4.9)	

Statistical test: Chi-squared test or Fisher's exact test. BMI: Body mass index; MI: Myocardial infarction; CABG: Coronary artery bypass graft; PCI: Percutaneous coronary intervention; MACE: Major adverse cardiac event (Death, Stroke, MI, PCI, and CABG); CVA: Cerebrovascular accident.

Discussion

The current study sought to examine the association between opium use and the incidence of MACE in patients undergoing PCI. Misconceptions regarding the purported beneficial effects of opium on longevity, as well as its supposed protective properties against CVD and myocardial infarctions, significantly contribute to an increased propensity for opium consumption among individuals.

The results of the present study revealed that BMI, percentage of hypertension, diabetes, and dyslipidemia were reduced, but the SYNTAX score and MACE were enhanced in opium-user CAD patients. The findings of a related study involving 325 patients scheduled for elective CABG indicated that individuals with opium addiction exhibited significantly lower BMI, prevalence of diabetes, and glucose levels (Aghadavoudi et al. 2015). It has been noted that the prevalence of diabetes, hypertension, and hemoglobin A1c (HbA1c) levels were markedly reduced in CABG patients who used opium compared to their non-opium-using counterparts. Conversely, the lipid profile did not reveal remarkable differences between two groups (Shirani et al. 2010). Additional studies also suggested that consumption of opium was related with a reduction in total cholesterol levels (Abbas et al. 2012). Despite the apparent reduction in certain cardiac risk factors associated with opium use, other research presents conflicting evidence (Baeradeh et al. 2023; Moezi et al. 2022). A study involving 304 patients with acute myocardial infarction reported no important differences in the rates of diabetes, hypertension, or hyperlipidemia between opium and non-opium users (Javadi et al. 2014). Furthermore, it has been indicated that prolonged opium use may adversely impact health by exacerbating conditions such as diabetes, dyslipidemia, and hypertension (Najafipour and Beik 2016).

These inconsistent findings may stem from differences in baseline conditions between opium and non-opium users, such as loss of appetite, malnutrition, and vitamin deficiencies reported among opium users (Kouros et al. 2010). Consequently, the reduced lipid profiles observed in some researches might be attributable to unhealthy diets or weight loss rather than a direct pharmacological effect of opium. Notably, a large population-based study conducted in Southern Iran reported no substantial association between opium consumption and lipid profiles, which supports the hypothesis that opium use does not directly influence lipid metabolism (Baeradeh et al. 2025).

Research indicates that opium use may contribute to an increased incidence of diabetes (Golozar et al. 2011). In a study by Sharafi et al. (Sharafi et al. 2014), a correlation was identified between history of diabetes and hypertension and opium use, which aligns with findings from an experimental study conducted by Mami et al. on rabbits (Mami et al. 2011). However, other investigations have reported no significant relationship between opium use and blood sugar levels or diabetes (ASGARI et al. 2005; Mahmoodi et al. 2012; Sadeghian et al. 2009). The discrepancies in these findings may be linked to factors such as the duration of opium use, dosage, method of opium use the duration of diabetes, and whether the study was conducted in controlled (animal) or uncontrolled (human) settings, as well as the sampling techniques employed. A study involving 5,900 individuals concluded that opium use did not have an important impact on the odds ratio (OR) for developing diabetes, hypertension, or hypercholesterolemia (Najafipour et al. 2015).

Similarly, the present study found no substantial relationship between opium use and mortality. A study focusing on 556 patients with myocardial infarction indicated no substantial relationship between opium use and mortality (Bafghi et al. 2005). Conversely, Golestan's cohort study suggested a remarkable association

between opium use and mortality across nearly all participant subgroups (Khademi et al. 2012a).

Our findings emphasize a substantial relation between opium use and MACE. A meta-analysis estimated that the odds ratio for CAD among opium users was 2.75 (Nakhaee et al. 2020). A retrospective study reported an odds ratio of 1.3 for CAD development among 2,405 opium users (Sadeghian et al. 2010), while a case-control study found this figure to be 3.8 (MASOUMI et al. 2010), indicating that opium consumption is a risk factor for CAD.

In the cohort study, which involved 50,045 participants, the risk of heart disease associated with opium use was quantified at 1.90 (1.57-2.29) (Khademi et al. 2012b). The study has highlighted the adverse cardiac effects of opium, categorizing it as a risk factor for carotid stenosis (Shirani et al. 2010). However, other research suggests that long-term opium use might decrease atherosclerosis and offer protection against ischemic cell damage (Marmor et al. 2004). Notably, one study found that anterior wall myocardial infarction was less prevalent among opium users (Dehghani et al. 2013). Long-term opium use is linked to elevated levels of several substances, including substance P, adenosine, and calcitonin (Bosshart 2011), which may exert cardio-protective effects. Nevertheless, the varying results across studies may stem from differences in substance type, the route of opium administration, and dosages administered. Chronic opium use can suppress both humoral and cellular immune responses, leading to low blood pressure, bradycardia, and respiratory depression, which can compromise myocardial oxygen supply and potentially increase infarct size and mortality (Bosshart 2011; Vallejo et al. 2004).

Ghazavi et al. research indicated that the higher serum levels of inflammatory mediators such as high-sensitivity C-reactive protein (CRP), alongside increased levels of certain complementary factors and nitric oxide in opium users who smoke compared to non-users. These findings suggest that opium may exert negative effects on the circulatory system (Ghazavi et al. 2013). Moreover, Asgari et al. observed that various risk factors associated with premature atherosclerosis, including, HbA1C, high-density lipoprotein cholesterol, factor VII, fibrinogen, apolipoprotein B (Apo-B), apolipoprotein A (Apo-A), and CRP, were elevated in opium users relative to non-users (Asgary et al. 2008). Finally, the opium receptors including kappa (κ), mu (μ), and delta (δ) receptors, interact with endogenous opioid-like ligands such as endorphins, dynorphins, and enkephalins, potentially producing varied effects on cardiac health (Headrick et al. 2015).

According to the findings of our study, the OR for cardiovascular events is elevated in patients with a history of type 2 diabetes. Hosseini et al. reported that diabetic opium users had a higher incidence of coronary artery involvement compared to their diabetic counterparts who did not use opium (Hosseini et al. 2011). Additionally, while the results indicated a higher OR for myocardial infarction in opium users with a history of diabetes, this finding did not reach statistical significance (Bafghi et al. 2005). Moezi et al. revealed that the OR for CVD was 87% higher in individuals with fasting blood sugar levels exceeding 126 mg/dL (OR: 1.87, 95% CI: 1.24-2.84, p=0.003) (Moezi et al. 2020). Another study also showed that the OR of CAD was 3.5 times higher in diabetic patients (Yoo et al. 2009). These findings suggest that CAD risk factors in diabetic patients—namely hyperglycemia, dyslipidemia, and insulin resistance—can contribute to endothelial dysfunction, promote platelet adhesion, and lead to abnormal coagulation processes (Momiyama et al. 2012; Srinivasan et al. 2016).

Our study also revealed that an increase in the SYNTAX score correlates with a heightened odds ratio for MACE, indicating a substantial association between

opium use and SYNTAX score. A study involving 381 patients showed that a higher SYNTAX score increased the risk of MACE by 3.07 times after regulating for ejection fraction and the number of stented vessels (HR: 3.07, 95% CI: 1.46-6.48, p=0.003) (Safarian et al. 2014). Furthermore, an elevation in the SYNTAX score corresponded with a 14% increased risk of cardiac events (Nam et al. 2011).

It is important to note that traditional opium users often smoked cigarettes, making smoking a potential confounding factor in this study. Various methods of opium consumption including inhalation and oral routes, may result in differing cardiovascular effects. Unlike pure opiates such as heroin, opium comprises a mixture of substances which may produce varied health impacts. There is a common belief that opium was purer and more effective in past years than it is currently; however, the purity of opium remains unmeasured in this investigation, presenting a limitation.

Additionally, some users consume opium in small quantities, comparable to that of a seed or lentil; however, the frequency of such consumption was not quantified in our study. Thus, it highlights the need for future research to delve deeper into these factors to obtain more reliable insights into the effects of opium on CADs. Limitations of our research include the small sample size of opium users, the lack of clarity regarding the method of administration (oral vs. inhalation), and a short follow-up duration.

Contrary to the popular belief that opium serves as a protective agent against various diseases, the results of the present study illustrate that opium use is associated with an increased odds ratio for cardiovascular events. Furthermore, a history of type 2 diabetes, dyslipidemia, and hypertension—known risk factors for CAD—was significantly linked to opium use. Additionally, an increase in the SYNTAX score was found to be related to cardiovascular events.

Acknowledgment

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Conflicts of interest

The authors declare that there are no conflicts of interest regarding this study.

Ethical Considerations

The study protocol was approved by the Ethics Committee of the Vice-Chancellery for Research and Technology of Birjand University of Medical Sciences.

Code of Ethics

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Authors' Contributions

Mahboobe Rafati: conceptualized the study, obtained the data, and prepared the manuscript. Mohammad Reza Khazdair: conceptualized the study, analyzing the data, prepared and revised the manuscript. Seyyed Ali Moezi, Toba Kazemi and Ehsan Shirvani: conceptualized the study, obtained the data, and helped to revision and edit the manuscript. Nahid Azdaki: is responsible for study design, drafting, and revising the manuscript. All authors read, and approved the final manuscript.

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