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**Coronary Artery Disease and The Prevalence of Opium
Consumption: A Systematic Review and Meta-analysis in
the Iranian Population**

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Abstract

Objective

The aim of this research was to investigate the prevalence of opium consumption among CAD patients.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations were followed when conducting this systematic review and meta-analysis. Two independent reviewers chose all observational studies (case-control, cohort, and cross-sectional studies). STATA software was used to determine the usage of opiates in CAD patients.

Results

A total of 7 studies including 14124 cases were included in the present study. The overall prevalence of CAD among addicted 16% (95% CI: 14%-17%) patients was significantly higher than the same percentage among non-addicted 6% (95% CI: 5%-6%) patients.

Conclusion

Our study's findings and previous research indicate that opioid usage may impact coronary artery disease when combined with other risk factors such as smoking, diabetes, high blood pressure, and hyperlipidemia. To assess the prognosis of patients, it is advised to examine opioid dependency combined with other risk factors.

Keywords: Coronary artery disease, opium, opiate, cardiovascular

Introduction

Heart attack (STEMI), unstable angina, coronary artery disease, and non-STEM fall under the category of acute coronary syndrome (1). Cardiovascular diseases continue to be the leading cause of mortality worldwide despite significant improvements in both preventative and treatment strategies. About 800,000 Americans are admitted to hospitals each year because of heart attacks. Younger males have a greater death risk from heart attacks than young women, and this rate rises as the left ventricular ejection fraction decreases (3). Studies carried out in Iran indicate that cardiovascular disorders are among the most prevalent among Iranians (4), accounting for one-third of all fatalities there (5). Iran's most prevalent addiction is drug addiction (6). The incidence of opium addiction is 0.5% worldwide (7), but in Iran, the general population has a 2.8% to 2.8% prevalence of drug usage, compared to 9.9% to 19% for those who have experienced an acute heart attack (8, 9). The assumption that using these medicines can help lower the risk of cardiovascular variables, including diabetes and blood pressure, is the main justification for this group's usage of narcotics (8, 10). According to research, opioids operate on potassium and calcium channels to generate hypotension, bradycardia, and vasodilation (11). Interleukin-6 and interleukin-1 receptor antagonist levels are greater in individuals with coronary artery disease, and interleukin-1 receptor antagonist levels are also higher in patients with opioid addiction than in non-opioid-dependent patients (12). Additionally, drug users had considerably higher levels of CRP, HbA1c, lipoprotein A, factor 7, fibrinogen, apB, AST, and ALT than non-users (9,13). Another study found a strong correlation between opium usage and cardiac arrhythmias following myocardial infarction, including atrial tachycardia, bradycardia, and atrial fibrillation (8). In contrast, long-term drug usage was linked to a reduction in the severity of cardiovascular disorders in another study (14). It is crucial to understand how opium affects many diseases, particularly heart ailments, given the relatively large population of drug addicts in Iran and the scant amount of studies on how opioid

addiction affects the cardiovascular system. As a result, research on how opium affects the frequency of coronary artery stenosis was done.

Method

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations were followed when conducting this systematic review and meta-analysis. In this study, concepts including opium, opioids, coronary heart disease, and coronary arteries are used together with other terms from the Medical Subject Headings (MESH) term. Cardiology, angiography, atherosclerosis, atherogenesis, vascular disease, myocardial infarction (MI), and ischemic heart disease up to August 10, 2022, major worldwide databases, including Web of Science, PubMed, and Scopus, were searched by two independent reviewers without regard to language or time frame.

Eligibility criteria

Two independent reviewers chose all observational studies (case-control, cohort, and cross-sectional studies). Additionally, relevant article references were manually sought. After focusing on the search technique and eliminating duplicates, filtering was carried out to find more pertinent articles. Studies that had nothing to do with evaluating the titles, abstracts, and full texts were then crossed from the list. Editorials, case studies, case series, review articles, conference papers, animal and laboratory research, and pieces with insufficient data are not permitted under the criteria.

Data extraction

A predetermined checklist was used to extract the data. Author's name, study date and location, sample size and sampling strategy for each group, details on the participant's age and gender, frequency of opium usage, and frequency of heart attacks are all provided. Additional data, including evaluation techniques, intervening factors, and each study's key findings, were

discovered and utilized for qualitative assessment. We could have reached out to the authors up to twice if further information about the survey was required. Two researchers carried out each step of the process—finding studies, choosing studies, and collecting data. A third researcher was brought in to remedy any issues with the article selection.

Statistical analysis

STATA software was used to determine the prevalence of CAD and the usage of opiates in CAD patients. To assess the studies' heterogeneity, the I-square test was performed. If $p < 0.05$, the results of Q tests were deemed

statistically significant. I^2 was also computed to gauge study variability. Begg's test was used to assess publication bias when considerable heterogeneity was found (results with more than 10 effect sizes).

Results

Out of 331 available studies, 131 articles were excluded. Of the 131 excluded studies, 17 articles did not have full text, 12 were review articles, 32 were letters to the editor, and 70 articles did not meet the study criteria. Among the remaining 19 studies, 7 studies met the study criteria. (figure 1).

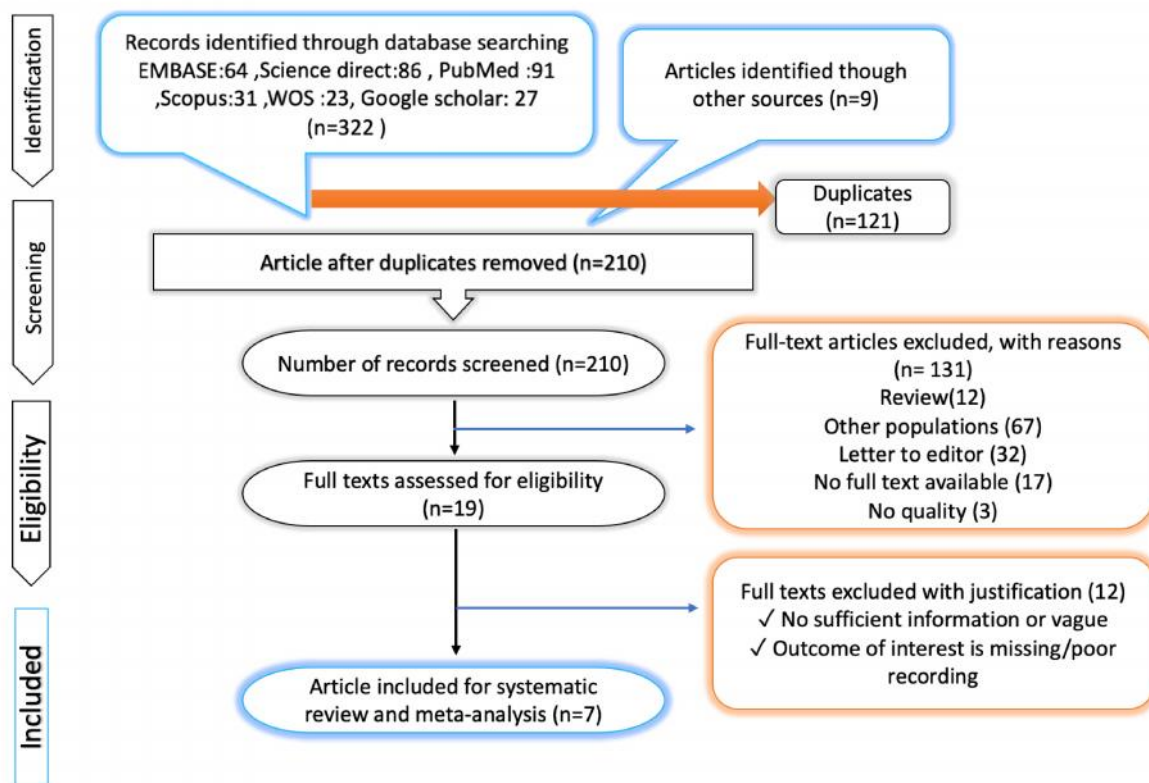


Figure 1. PRISMA flow diagram

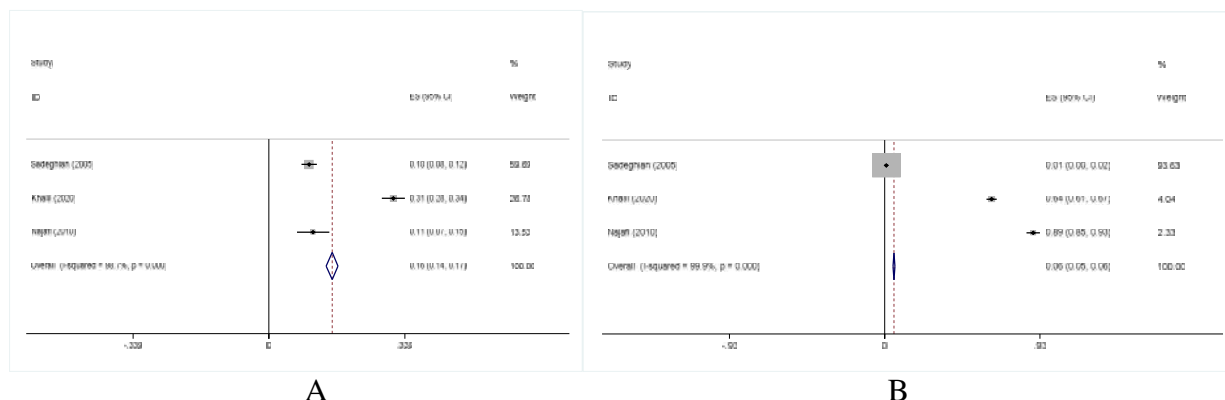
A total of 7 studies including 14124 cases were included in the present study. The overall prevalence of CAD among addicted 16% (95% CI: 14%-17%) patients was

significantly higher than the same percentage among non-addicted 6% (95% CI: 5%-6%) patients (table 1, figure 2).

Table1. Characteristics of the included studies regarding the association between ischemic cardiac disease and addiction

Author	Year	Age	Male/female	Design	City	Sample size	Prevalence in addicted				Prevalence in non-addicted				CAD	
							CAD	SA	NSA	MI	CAD	SA	NSA	MI	Opium consumption	No opium use
Aghavandi	2014	58.76±9.02	N/A	Cross-sectional	Isfahan	325	114 (97.4)	16 (13.7)	92 (78.6)	54 (46.2)	195 (97.0)	34 (16.9)	146 (72.6)	92 (45.8)	N/A	N/A
Sadeghian	2005	57.5±10.3	64/36	Cross-sectional	Tehran	2405	82.7%	N/A	N/A	N/A	93.4%	N/A	N/A	N/A	N/A	N/A
Masoomi	2010	57±3.4	69/22	Case-control	Kerman	137	79%	N/A	N/A	N/A	50%	N/A	N/A	N/A	N/A	N/A
Rostamzade	2016	59.65±16.6	N/A	Cross-sectional	Orumieh	95	N/A	N/A	15.3%	N/A	N/A	N/A	11.5%	N/A	N/A	N/A
Sadeghian	2005	49.48±4.5	387/533	Cross-sectional	Tehran	940	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	98/940	11/940
Khalili	2021	49.91±9.56	465/5335	Cross-sectional	Rafsanjan	9990	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	313 (35.98)	557 (64.02)
Najafi	2010	N/A	N/A	N/A	Tehran	232	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	26/232	206/232

Figure 2. Comparison of the prevalence of CAD among opium-addicted (A) and non-addicted(B) patients



Discussion

Opium addiction is particularly common among people with ischemic heart disease. In research conducted in Kerman, Iran, by Koros et al., it was discovered that opium users' fasting blood sugar levels (FBS) were considerably lower than those of the control group (14). In other research, opium users and non-users had significantly different histories of diabetes and blood sugar levels before and after surgery, and the proportion of diabetic patients was lower in the opium user group. Additionally, opium users had much lower blood sugar levels before and after the procedure than non-users. These findings could be an indication that opium lowers blood sugar levels.

According to Shirani et al., opium users had significantly lower blood pressure rates and diabetes mellitus than non-users. Additionally, opium users had considerably lower fasting blood glucose and hemoglobin A1c (HbA1c) values. However, neither group's lipid profiles significantly differed from one another (15). HbA1c levels were greater in addicted men than in the control group, according to Karam et al., although there was no appreciable difference in FBS levels. Moreover, considerably less high-density lipoprotein cholesterol (HDL-C) was present in addicted men (16). These studies' different sample sizes might be the cause of their differences. Previous research looked at how opioids (opium) affected elements that contribute to atherosclerosis, such as lipid profiles. In

research using animal models, Mohammadi et al. found that non-addicted and addicted rabbits have significantly different levels of total cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Furthermore, rabbits with addiction had much greater levels of atheromatous plaque formation. They claimed that opium use could exacerbate the development of atherosclerosis linked to elevated cholesterol, which primarily impacts the lipid profile (17).

Opium use is successful in causing atheromatous plaques, according to studies by Davoudi et al. in 2005, [18] Sadeghian et al. in 2007, [19] Azimzadeh et al., Sarwar et al., and Spinella in 2001 [21]. Across all opium use routes, there was, as predicted, a connection between opium use and cardiovascular illness. Another finding from earlier research showed that opium use orally was linked to an increased risk of cardiovascular disease (19-21).

Contrary to popular belief, Najafipour et al. found that opiate use has no beneficial impact on blood lipid, blood pressure, or diabetic profiles (9). In our nation, opium addiction is a serious public health issue. On the other hand, the list of fatalities and complications in Iran is topped by those brought on by CAD (22). Numerous scientists are looking for a relationship between opium, CAD, and the atherosclerosis phenomena. According to earlier research, opium addiction affects 10% of people who have had coronary artery bypass surgery and 13% to 20% of those

who have had a heart attack (23). Physiopharmacological research back up the impact of opium on the cardiovascular system, despite clinical uncertainty regarding the connection between opium addiction and CAD (22, 23).

There are various things to remember: 1. The approaches and procedures used to perform the research included in this meta-analysis varied. For instance, these early research varied in how they matched case-control groups and handled adjusted confounders during odds ratio estimations. There is usually an intervening element, which is one of the traditional risk factors for cardiovascular disease when it comes to the impact of opium on the circulatory system. In addition, the medicine can be administered inhalationally, orally, or intravenously, each of which affects the drug's absorption and blood levels differently. As a result, this point should also be taken into account. The cardiac effects of opium have been described for various opium kinds and intake techniques in a cohort study involving 50,045 individuals (24). Additionally, several studies did not list alcohol, tobacco, or nicotine/cigarettes as potential confounders, which restricts the generalizability of the findings.

Studies on opium undertaken in various regions of the world may provide varied results since illicit opium is not a pure material and contains contaminants like lead, particularly in Iran. These elements must be taken into account both in the design of future investigations and in the analysis and interpretation of the findings. This study can help create new plans and tactics to stop or reduce opium use in nations with high opium consumption rates or those on opium transportation routes.

Conclusion

Our study's findings and previous research indicate that opioid usage may impact coronary artery disease when combined with other risk factors such as smoking, diabetes, high blood pressure, and hyperlipidemia. To assess the prognosis of patients, it is advised to examine

opioid dependency combined with other risk factors.

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