Original Article

Does Opioid Addiction Influence Clinical and Angiographic Outcomes in STEMI Patients Undergoing Emergency PCI?

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Abstract

Background: Despite recognizing the traditional coronary artery disease (CAD) risk factors, some secondary factors, such as opioid substance abuse, have to be considered. We aimed to assess the relationship between opioid consumption and emergency percutaneous coronary intervention (PCI) revascularization results, according to Thrombolysis in Myocardial Infarction (TIMI) flow and in-hospital survival outcomes in ST-elevation myocardial infarction (STEMI) patients.

Materials and Methods: This case–control study was conducted on 186 patients (93 patients in each group) with acute STEMI, who were referred to Chamran Heart Center, Isfahan, Iran. Opioid addiction was diagnosed by patients' records and confirmed by conducting an interview based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria. Patients in both groups were evaluated and compared for angioplasty results based on the TIMI flow grade and in-hospital cardiovascular events and complications.

Results: Ninety-one patients (97.84%) of each group were male, and opioid-addicted patients were younger than the non-opioid users (52.95 9.91 vs. 57.90 12.17, $P = 0.003$). Among the CAD risk factors, prevalence of dyslipidemia was significantly higher in non-opioid users, whereas cigarette smoking was higher in opioid-addicted patients ($P < 0.050$). There was no significant difference between the two groups regarding pre- and post-procedural myocardial infarction complications as well as mortality rate ($P > 0.050$). Also, there were no significant differences between the opioid and non-opioid users regarding TIMI flow grading, and successful PCI rate based on achieving TIMI III was 60.21% versus 59.1% in opiate-dependent and non-opioid users, respectively ($P = 0.621$).

Conclusion: Opioid addiction has no effects on post-PCI angiographic results and in-hospital survival outcomes in STEMI patients which undergoing emergency PCI.

Keywords: Myocardial Infarction, opioid, PCI, TIMI flow

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Introduction

Cardiovascular diseases, especially acute coronary syndrome (ACS), is currently the most common cause of death worldwide and in our country, Iran.[1] The main and known traditional risk factors for coronary artery diseases (CADs) are diabetes mellitus, hypertension, dyslipidemia, cigarette smoking, and immobility, as well as positive family history.[2] But since Iran is located in the main pathway of opium transit and its people use opiates as first-rated substance abuse,[3,4] it is important to know the positive and negative effects of opioids on the cardiovascular system. The prevalence rate of

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opium addiction is about 2%–3% among Iranian population, and it was estimated to be about 10%–20% in acute myocardial infarction (MI) patients.[5,6] In addition to euphoria and relaxation, one of the most important reasons for opioid abuse in our population is misconception on the preventive and ameliorating effects of opiates in CAD risk factors such as hypertension and diabetes mellitus.[5,7] However, in the world of science and research, this is also known as a challenge; and some studies have revealed worsening or null effects of opiates on CAD and its risk factors,[5,6,8-12] whereas others believe that opioids have beneficial effects in preventing ischemic heart diseases.[13,14] A recent review article revealed that opium use does not protect against or improve cardiovascular problems.[15] In any case, knowing the relationship between opioid use and cardiovascular diseases is not the aim of this study, and we are looking at its effect on the treatment process of ACS patients.

As we know, acute ST-segment elevation myocardial infarction (STEMI) is the most important component of ACS, which requires prompt and timely treatment to establish coronary blood flow.[16] Percutaneous coronary intervention (PCI) is considered as gold standard therapy for coronary blood flow restoration and reperfusion of ischemic myocardium, which decreases mortality and morbidity as well as increases survival in patients with STEMI.[17]

Since there is insufficient knowledge regarding the effects of opioids on coronary reperfusion in STEMI patients, in this study, we aimed to assess the relationship between opiate consumption and PCI revascularization outcomes, according to Thrombolysis in Myocardial Infarction (TIMI) flow and in-hospital survival results on the consequences of emergency coronary angioplasty.

Materials and Methods

Study type and population

In our cross-sectional case–control research, the study population consisted of patients aged between 18 and 85 years with acute STEMI diagnosis, who were referred for primary or rescue PCI to Chamran Heart Center, Isfahan, Iran, which is the largest referral hospital in central Iran, from January 2019 to August 2019. STEMI diagnosis was based on typical chest pain with onset time less than 24 h and at least 1 mm ST-segment elevation in two or more contiguous leads and elevated cardiac biomarkers simultaneously.[18] Patients with renal dysfunction (glomerular filtration rate 60 ml/min and less or serum creatinine above 2 mg/dl), impaired liver function, severe infection, autoimmune and inflammatory diseases, subjects had cardiac arrest and received cardiopulmonary resuscitation prior to the intervention, and patients who were treated only by medication or candidates for coronary artery bypass graft (CABG) after diagnostic CAG had been excluded from the study. Patients were classified into two groups including opioid addict group as the case group and non-opioid user as the control group. Opioid addiction was defined on the basis of the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria for substance dependence as regular consumption of inhalatory opium more than three times per week and/or oral opium daily.[19] All patients in the case group consumed opioid regularly before and during hospitalization (injection as needed) for withdrawal syndrome avoidance. The control group was selected in equal number to the case group after adjusting for sex, diabetes, and cardiogenic shock. The study protocol was reviewed and approved by the Chamran Heart Center Ethics Committee, affiliated with Isfahan University of Medical Sciences. Written informed consent was obtained from all patients.

Study variables

The main endpoint was revascularization outcome based on TIMI flow grade. TIMI flow grade 0 is defined as no perfusion, grade 1 as penetration without perfusion, grade 2 as partial perfusion, and grade 3 as complete perfusion.[20] Successful PCI was also investigated by angiographic definition as residual stenosis less than 20% in the presence of grade 3 TIMI flow without major intimal dissection. All angiographic views were assessed by a blinded interventionist. The secondary endpoints that included in-hospital survival outcomes were major adverse cardiac events (MACEs) including death, MI, and ischemic stroke.

Patients' basic characteristics including age, gender, and past medical histories such as hypertension (systolic blood pressure [SBP] 140 or diastolic blood pressure [DBP] 90 or receiving antihypertensive drugs), diabetes mellitus (fasting blood sugar [FBS] 126 or random plasma glucose test 200 or hemoglobin A1c [HbA1c] 7% or receiving oral diabetic medication/insulin), dyslipidemia (total cholesterol 200 mg/dl or low-density lipoprotein [LDL] 130 mg/dl or triglyceride 150 mg/dl or high-density lipoprotein [HDL] 40 mg/dl [male] and 50 mg/dl [female] or using antihyperlipidemic agents), stroke, peripheral artery disease (defined as acute or chronic obstruction of arteries supplying the lower or upper extremities), heart failure, and current cigarette smoking were extracted from hospital record files and patient interview. Opioid consumption data were obtained by face-to-face interview and included self-reported type of substance, method of use, and dose and duration of consumption.

Angiographic and procedural basic data such as time from the onset of symptoms to the performance of PCI, level of MI, type of PCI (primary or rescue), target vessel, CAD severity, and baseline TIMI flow grade were also investigated. Electrical and mechanical cardiac complications in three time intervals, including preintervention, during the first 24 h of the intervention, and after the first 24 h of PCI until the end of hospitalization, were extracted from the patients' hospital records.

Statistical analysis

Quantitative variables were reported as mean standard deviation (SD) and number (percentages) for the categorical variables. The groups were compared using the Student's *t*-test for continuous variables and the Chi-square test (or Fisher's exact test if needed) for categorical variables. Odds

ratio with 95% confidence interval for the association between opioid addiction and PCI angiographic results, in adjusted and non-adjusted models, was calculated. Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 25 (SPSS, Inc., Chicago, IL, USA), and *P* values of 0.05 or less were considered statistically significant.

Results

Of the patients admitted with STEMI diagnoses during the mentioned interval, 110 had opioid consumption records. Ten of these had not undergone coronary angioplasty (World Health Organization [WHO] candidates for only medical treatment or candidates for CABG) and were excluded from the study. Seven patients who denied opioid use in the interview were also excluded. Of the remaining 93 patients who were enrolled in the study, 91 (97.84%) were male and two (2.15%) were female. The control group was randomly selected (93 patients) after sex matching [Figure 1]. Given that diabetes and cardiogenic shock have significant effects on coronary angioplasty results, the two groups were also matched for these variables.

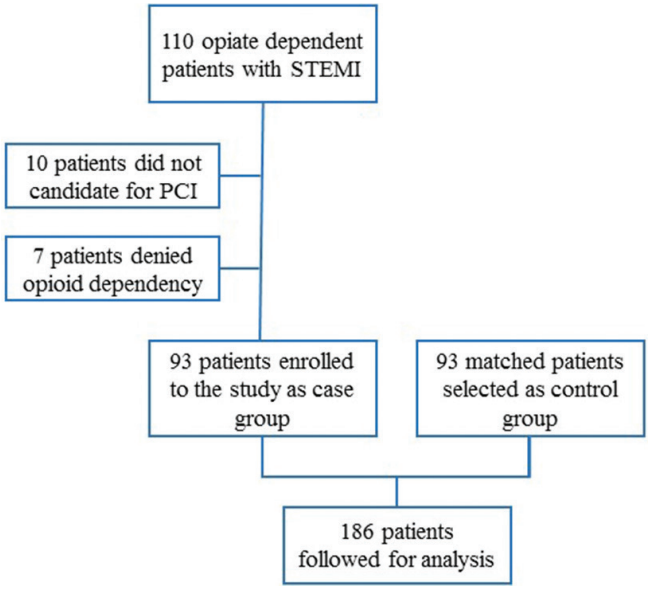

Figure 1: Study design. PCI = percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction

Opioid-addicted patients were younger than the non-opioid users (52.95 9.91 vs. 57.90 12.17, $P = 0.003$). The frequency distribution of basic and clinical variables in both groups is presented in Table 1. Among the CAD risk factors, only dyslipidemia and cigarette smoking had significant differences between the groups ($P < 0.050$), in such a way that prevalence of dyslipidemia was higher in non-opioid users, whereas cigarette smoking was higher in opioid-addicted patients. Hypertension prevalence was also nonsignificantly lower in the case group ($P = 0.068$). There were no significant differences in the prevalence of stroke, PAD, and heart failure between the two groups ($P > 0.050$). There was no significant difference between the two groups in hemoglobin level and platelet count ($P > 0.050$), but creatinine level was lower in opiate-dependent group (1.22 vs. 1.07, $P = 0.006$).

Opiate-dependent group patients consumed different forms of opioid, which consisted of 84 (90.32%) cases of opium (inhalation and orally), seven (7.52%) cases of methadone syrup, and two (2.15%) cases of tramadol tablets. Most commonly consumed form of opium was inhalatory with 79 (94.04%) cases. The opioid consumption doses were calculated based on gram 1.98 2.77 and morphine equivalent dose (MED) 0.29 0.40. The mean (SD) of opioid usage duration was 11.74 (9.03) years.

The time interval from the onset of pain to emergency PCI in the dependent and non-dependent groups is plotted in Figure 2 ($P > 0.050$). In both groups, the most common time interval from pain onset to PCI was between 3 and 6 h.

Since patients with coronary thrombotic lesions were receiving injectable antiplatelet drug, eptifibatide, as a IIb/IIIa inhibitor agent during angioplasty, the two groups were also compared in this regard. No difference was found between opiate-dependent group (39 [41.93%]) and non-dependent group (50 [53.76%]) ($P = 0.142$). The mean (SD) of the left ventricular ejection fraction (EF) was 40.22 (11.17) and

Table 1: Patients' basic and clinical characteristics

Variable	Non-opioid user (*n*=93)	Opioid addict (*n*=93)	*P*
Age (years), mean (SD)	57.90 (12.17)	52.95 (9.91)	0.003
Gender (male/female), *n* (%)	91 (97.84)/2 (2.15)	91 (97.84)/2 (2.15)	0.690
Hypertension (yes), *n* (%)	41 (44.08)	28 (30.10)	0.068
Diabetes mellitus (yes), *n* (%)	15 (16.12)	15 (16.12)	-
Dyslipidemia (yes), *n* (%)	16 (17.20)	6 (6.45)	0.039
Stroke (yes), *n* (%)	5 (5.37)	3 (3.22)	0.745
Peripheral artery disease (yes), *n* (%)	0 (0)	2 (2.15)	0.825
Heart failure (yes), *n* (%)	1 (1.07)	0 (0)	0.319
Current smoking (yes), *n* (%)	57 (61.29)	81 (87.09)	0.0001
Hemoglobin level (g/dl), mean (SD)	14.79 (1.45)	14.91 (1.85)	0.156
Platelet count (10^3/µl), mean (SD)	205.96 (60.71)	208.57 (72.12)	0.934
Creatinine level (mg/dl), mean (SD)	1.22 (0.38)	1.07 (0.20)	0.006

Table 2: Procedural and angiographic data

Variable	Non-opioid user (*n*=93)	Opioid addict (*n*=93)	*P*
CAD severity, *n* (%)			
1 VD	43 (46.23)	44 (47.31)	0.994
2 VD	37 (39.78)	34 (36.55)	
3 VD	12 (12.90)	15 (16.12)	
Left main	1 (1.07)	0 (0)	
PCI setting, *n* (%)			
Primary	59 (63.44)	55 (59.13)	0.548
Rescue	34 (36.55)	38 (40.86)	
MI level, *n* (%)			
Extensive	25 (26.88)	31 (33.33)	0.714
Anterolateral	15 (16.12)	6 (6.45)	
Lateral	5 (5.37)	3 (3.22)	
Anteroseptal	11 (11.82)	8 (8.60)	
Septal	0 (0)	0 (0)	
Anterior	2 (2.15)	4 (4.30)	
Inferior-posterior-lateral	8 (8.60)	7 (7.52)	
Inferior-posterior	6 (6.45)	12 (12.90)	
Posterior	0 (0)	0 (0)	
Inferior	16 (17.20)	18 (19.35)	
Inferior RV	5 (5.37)	4 (4.30)	
Isolated RV	0 (0)	0 (0)	
Culprit vessel, *n* (%)			
Left main	1 (1.07)	1 (1.07)	0.130
LADA	52 (55.91)	44 (47.31)	
Diagonal	1 (1.07)	3 (3.22)	
LCX	3 (3.22)	14 (15.05)	
OM	5 (5.37)	4 (4.30)	
RCA	28 (30.10)	24 (25.80)	
PDA	2 (2.15)	2 (2.15)	
PLV	1 (1.07)	1 (1.07)	

CAD=coronary artery disease, LAD=left anterior descending artery, LCX=left circumflex, OM=obtuse marginal, MI=myocardial infarction, PCI=percutaneous coronary intervention, PDA=posterior descending artery, PLV=posterior left ventricle, RCA=right coronary artery, RV=right ventricle, VD=vessel diseases

39.24 (11.86) in opiate-dependent and non-dependent groups, respectively ($P = 0.223$). CAD severity in most of the patients in both groups was single vessel diseases [Table 2]. There was no significant difference between groups regarding the MI level and the culprit vessel ($P > 0.050$) [Table 2]. The most common MI level (according to surface electrocardiogram [ECG]) in both groups was extensive anterior MI, and the most common culprit vessel in both groups was left anterior descending artery (LAD). Patients were evaluated for electrical and mechanical complications at three time intervals, before PCI, during the first 24 h after PCI, and after the first 24 h until discharge, and there was no significant difference between the two groups in any of the three time intervals ($P > 0.050$) [Table 3]. There was no report about mechanical complications including free wall rupture, ventricular septal rupture, severe mitral regurgitation, and tamponade.

There were no significant differences between the opioid and non-opioid users regarding TIMI flow grading before and after the PCI and TIMI delta changes ($P > 0.050$) [Table 4]. Successful PCI rate based on achieving TIMI III was 60.21% versus 59.1% in opiate-dependent and non-opioid user groups, respectively ($P = 0.621$).

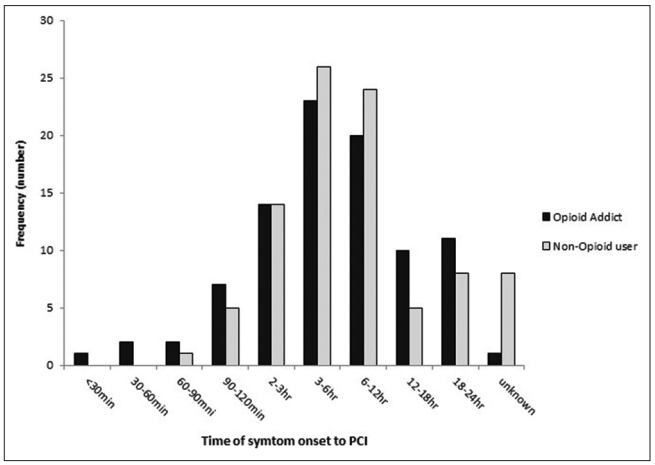

Figure 2: Time interval from the onset of pain to emergency PCI. PCI = percutaneous coronary intervention

To assess the relationship between opioid consumption and successful PCI angiographic results in a binomial variable (TIMI flow = III and TIMI flow <III), odds ratio was calculated in crude and adjusted models. Results of these analyses showed that there was no significant positive or negative association between the opioid addiction and successful PCI results (according to TIMI flow III) ($P > 0.050$) [Table 5].

Discussion

Opioid substance abuse has been a major problem in many countries, and there is still a controversy about the potential benefits or harms of opiates on coronary heart disease. Previous studies have focused more on the role of opium addiction in CADs extension and MI clinical outcomes and complications. For the first time, in this study, we investigated the opioid consumption effects on post-PCI angiographic results (based on TIMI flow grading) in STEMI patients which undergoing primary or rescue coronary. Our results indicated that post-procedural TIMI flow had no significant difference in opioid-addicted patients when compared to non-opioid users. The PCI success rate (defined as TIMI flow grade III) was also almost the same in both populations, and there was no significant association between the opioid addiction and successful PCI results. In our study, opioid-dependent patients were younger than non-opioid users, and dyslipidemia was less frequent and cigarette smoking was more frequent. In Roohafza *et al.*'s[21] study also, opium-dependent patients were younger and their age was lower at the cardiovascular event time. As a point of interest, they reported that opium did not improve cardiovascular risk factors or post-MI mortality and morbidity. Improved cardiac risk factors such as dyslipidemia and hypertension were found in Mirzaiepour *et al.*'s study,[22] in contrast to other studies.[23] Smoking was more common in

Table 3: Comparison of pre- and post-procedural complications and death between the two groups

Variable	Non-opioid user ($n=93$)			Opioid addict ($n=93$)		
	Before PCI	First 24 h after PCI	After 24 h of PCI	Before PCI	First 24 h after PCI	After 24 h of PCI
Electrical complications (yes), *n* (%)						
Ventricular tachyarrhythmia	11 (11.82)	5 (5.4)	2 (2.1)	12 (12.90)	7 (7.5)	3 (3.2)
Atrial tachyarrhythmia	1 (1.1)	2 (2.1)	1 (1.1)	1 (1.1)	2 (2.1)	0 (0)
Bradyarrhythmia	3 (3.2)	3 (3.2)	1 (1.1)	4 (4.3)	1 (1.1)	0 (0)
Cardiogenic shock (yes), *n* (%)	2 (2.1)	3 (3.2)	1 (1.1)	2 (2.1)	0 (0)	0 (0)
Death (yes), *n* (%)	0 (0)	4 (4.3)	1 (1.1)	0 (0)	1 (1.1)	1 (1.1)

*There was no statistically significant difference between the groups ($P>0.050$)

Table 4: PCI outcomes according to TIMI flow variables

Variable	Non-opioid user ($n=93$)	Opioid addict ($n=93$)	*P*
TIMI flow (before the procedure), *n* (%)			
0	49	58	0.290
1	12	10	
2	18	9	
3	14	16	
TIMI flow (after the procedure), *n* (%)			
0	2	3	0.771
1	15	6	
2	20	29	
3	56	55	
TIMI flow changes (delta), mean (SD)	1.43 (1.28)	1.64 (1.26)	0.270
PCI success, *n* (%)	56 (60.21%)	55 (59.10%)	0.621

PCI=percutaneous coronary intervention, SD=standard deviation, TIMI=Thrombolysis in Myocardial Infarction

Table 5: Association between opioid addiction and TIMI flow grade (unadjusted and adjusted hazard ratio)

Analysis	Odds ratio	95% confidence interval	*P*
Model 1	1.04	0.58-1.87	0.88
Model 2	0.93	051-1.71	0.82
Model 3	0.93	0.48-1.79	0.82

TIMI=Thrombolysis in Myocardial Infarction. Model 1: crude model; Model 2: age-adjusted model; Model 3: adjusted model for age, hypertension, dyslipidemia, smoking, and creatinine level

addicted patients in most of the studies.[22-26] CAD severity, MI level, and culprit vessel distribution in our study showed no prominent difference between opioid users and non-users, and most of the patients were single vessel with extensive MI and LAD involvement. These data agree with the findings of Khosoosi *et al*.,[25] which showed no significant difference in terms of infarction type and extension between the addicts and nonaddicts. In contrast to our results, Dehghani *et al*.[24] indicated that addicted patients had a lower incidence of anterior MI that it was associated with higher primary mortality. In the study of Mirzaiepour *et al*., opioid addiction was a strong risk factor for arrhythmia after acute MI and the prevalence of tachycardia and atrial fibrillation was significantly higher in opioid-dependent patients. In our study, ECGs in both groups were also reviewed and there was no significant difference in dysrhythmias at any of the three follow-up intervals. In addition to dysrhythmia, we also evaluated the MI mechanical complications including ventricular septal and free wall rupture, severe mitral regurgitation, and tamponade in which on cases were occurred. Like our findings, there was a consensus among the studies in that there is no association between opioid addiction and MACE and in-hospital mortality.[21,24,27,28] Also, a recent study by Mousavi *et al*.[29] revealed that in-hospital and 6-month outcomes in opium-addicted patients who presented with STEMI were not significantly different in comparison with non–opium-addicted patients.

Limitations

Our study had some limitations. Sample size was small, and we had no follow-up period. The information on the dose and duration of opioid consumption were inaccurate, given that it was obtained from interview. Another limitation of the study is the presence of confounding variables such as family history, smoking, and hyperlipidemia.

Conclusion

According to this study, opioid addiction has no effects on post-PCI angiographic results (based on TIMI flow grading) and in-hospital survival outcomes in STEMI patients which undergoing primary or rescue PCI.

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Conflicts of interest

There are no conflicts of interest.

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