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RESEARCH ARTICLE

Morphine Use Did Not Eliminate the Effect of Pain on Complications After Acute Myocardial Infarction

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Abstract:

Background:

Patients with Acute Myocardial Infarction (AMI) are usually present complaining of severe chest pain. This pain results from an imbalance between oxygen supply and demand, leading to severe complications. Different guidelines recommend using Morphine as a drug of choice for treating this pain.

Objective:

This study aimed to check the effect of chest pain and Morphine use on complications rate after AMI.

Methods:

This was a prospective observational study with a consecutive sample of 300 patients with AMI. Data were collected by direct patients interview and medical records review in the emergency departments & Intensive Care Units (ICU). Any complication developed within the hospital stay and after AMI was recorded. All correlated variables were analyzed using the binary logistic regression model.

Results:

The sample included 176 (58.7%) men and 124 (41.3%) women with a mean age of 56.92±12.13 years. A total of 83 patients (27.7%) developed one or more in-hospital complications. Acute recurrent ischemia was the most frequent complication; 70 (23.3%). Severe chest pain (≥ 7), duration of chest pain (more than 5 minutes), history of previous MI, and history of hypertension increased the occurrence of complications by 13%, 7%, 63%, and 25%, respectively. However, the use of Morphine did not have any protective effect against the development of these complications.

Conclusion:

The severity and duration of chest pain increased the occurrence of complications. Morphine administration did not have any protective effect against the development of these complications. Thus, it is recommended to update different policies and guidelines to use other types of chest pain relief methods, *e.g.*, treating the underlying cause of chest pain and addressing the imbalance between oxygen supply and demand.

Keywords: Chest pain, Morphine, Acute myocardial infarction, Complications, Cardiovascular diseases, Coronary heart disease.

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1. INTRODUCTION

Cardiovascular Diseases (CVDs) are the leading cause of death globally [1]. In Jordan, CVDs cause about 25% of all deaths [2]. One of the most common CVDs is Coronary Heart Disease (CHD) worldwide. Although treatment and control strategies for CHD are progressing, there is still a high rate of CHD incidence in the world. It is expected that by the year 2030, CHD will be a significant contributing factor to death nationwide [2]. In addition, statistics revealed that CHD has the peak mortality rate in both low- and high-income countries [3]. Accordingly, death rates will increase to above 25 million cases [4].

One of the acute coronary syndrome's most common clinical manifestations is acute ischemia, leading to severe chest pain. Furthermore, this chest pain can be caused by an

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imbalance between the metabolic requirements (oxygen demand) and oxygen supply [5, 6]. This pain might lead to additional secretion of catecholamines and other physiological cascades, worsening the symptoms and leading to lethal complications (*i.e*., acute recurrent ischemia, ventricular tachycardia, and ventricular fibrillation), which typically happen in the first 48-72 hours after AMI or even as early as in the first 20 minutes after AMI onset [6 - 9].

To control the consequence of ischemic chest pain on the complications, this chest pain should be controlled to prevent worsening the associated symptoms that may lead to lethal complications [7 - 10]. Traditional methods to handle this pain are either to treat the underlying cause or treat the pain itself. Treating the underlying cause might include using the following: antiplatelet such as aspirin, anticoagulation like heparin, nitrates, and beta-blockers [10, 11]. Treating pain is usually done by different analgesics, including Morphine and NSAIDs. Morphine is considered a medication of high quality to treat chest pain associated with AMI [12]. American College of Cardiology (ACC)/ AHA guidelines for managing patients with STEMI [10, 13] stated that in the lack of a history of an allergic reaction, intravenous (IV) morphine sulfate is the favored drug for pain relief because it decreases the cardiac workload resulted from the cardiac attack, produces a stimulation effect on the histamine-mediated processes, and reduces the oxygen demand of myocardial muscle [13 - 15].

Morphine works by lessening the pain effects associated with myocardial tissue ischemia and offers anxiolytic effects that help inhibit the anxiety resulting from the attack. Moreover, a vasodilatation effect of Morphine reduces both pulse and blood pressure, thus, decreasing the preload of cardiac demands [6, 12]. However, the use of Morphine in AMI treatment is questionable due to the lack of differences between the experimental and the control groups [6, 7, 13]. Furthermore, recent research found no difference in chest pain and complications between those who received and did not receive Morphine [12]. Again, no significant improvement was linked to the use of Morphine. Additionally, it was shown that patients receiving morphine treatment in isolation or alongside other drug therapy (like nitro-glycerine) had higher mortality rates, especially among NSTEMI-patients [16].

Internationally, AMI is one of the top medical disorders with high morbidity and mortality rates. Following the AHA guidelines, most healthcare providers in clinical settings use Morphine to manage the chest pain of AMI [6, 17]. Nevertheless, it is essential to mention here that cardiology scholars reported that such guidelines were only established based on experts' opinions [6, 8, 12]. Therefore, future research in CVDs should be conducted to give an evidence-base for (using/not using) Morphine among this population. Recent studies examine the use of Morphine to control pain in the early phase after AMI [6, 7, 9]. Therefore, the purpose of the study was to assess the effect of chest pain and the use of Morphine on the complications rate after AMI.

1.1. Research Hypotheses

Hypothesis one: Patients with severe chest pain (pain score ≥ 7) will have higher complication rate than other patients (mild and moderate). Hypothesis two: After controlling socio-demographics (age, gender, smoking status) and clinical characteristics (history of Diabetes Mellitus (DM), Hypertension (HTN), previous MI, previous angina, stent use, previous Coronary Artery Bypass Graft (CABG), pain duration, morphine use, beta-blocker use, nitrate, and thrombolytic use), pain scores will be an independent predictor for complications after AMI. Hypothesis three: After controlling socio-demographics (age, gender, smoking status) and clinical characteristics (history of DM, HTN, previous MI, previous angina, stent use, previous CABG, pain duration, pain severity, beta-blocker use, nitrate, and thrombolytic use) morphine use will be an independent predictor for complications after AMI.

2. MATERIALS AND METHODS

2.1. Research Design, Sample, and Setting

A prospective observational design was used in this study. The accessible population of interest was all patients with STEMI visiting Emergency Departments (ED) in four hospitals (one from each sector: Royal Medical Services (RMS), teaching, private, and governmental) from July-October, 2020.

Intended participants were selected using the consecutive sampling technique. All patients diagnosed with STEMI and met the eligibility criteria were approached (a confirmed diagnosis of STEMI evidenced by electrocardiogram changes and elevated cardiac enzymes, and being older than 18 years) until the needed sample size was reached (Fig. **1**). If the patient developed in-hospital complications before measuring chest pain or receiving Morphine in ED, they were excluded from the study. This aimed to discover the longitudinal, cause-and-effect aspect of the medical problem. Moreover, if patients were hemodynamically unstable, they were excluded from the study.

The required sample size was determined by power analysis using G* power software. The following assumptions were used: (a) medium effect size of 0.25, (b) a significance level of $\alpha < 0.05$, (c) power of 80%, and (d) statistical tests used to test the research hypotheses; one-way ANOVA for hypothesis one, and the logistic regression for hypotheses two and three. For the logistic regression, 27% as an estimated incidence rate of complications was used [18] in addition to 14 independent variables. Based on these assumptions and statistical tests, the required sample size was 250. However, about 15% of the calculated sample size was added to create a more representative sample and overcome the suspected attrition and incomplete questionnaires that might occur. Therefore, the total sample size was 300 participants.

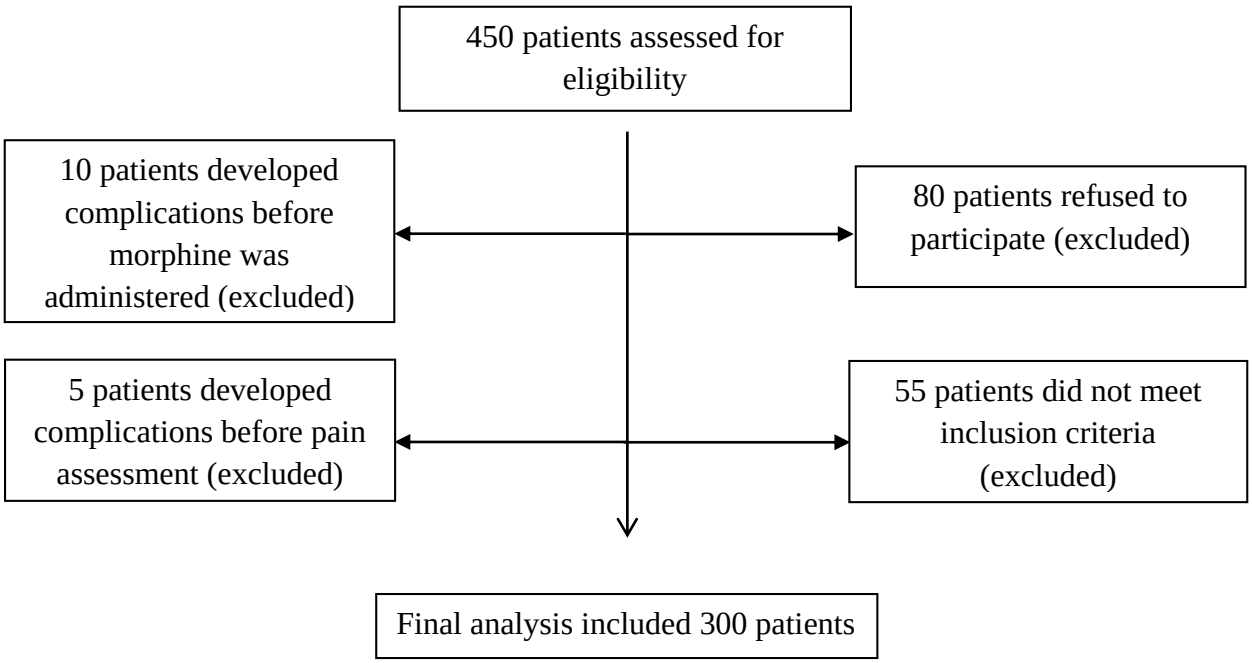

Fig. (1). Patient flow diagram.

2.2. Ethical Considerations

Ethical approvals were obtained from all IRB committees before data collection started (IRB#: Faculty 2019-2020- 4-4). Participants were fully informed about the nature, purpose, expectations, significance, benefits, risks, and type of required data, including the review of their medical records after discharge. Participation was voluntary, and informed consent was obtained before data collection started. All collected data were saved securely in a protected place keeping confidential and sharing only with the Principal Investigator and the co-investigators.

2.3. Procedures

After ethical approvals from all sites were gained, the PI contacted the head nurse of each selected ED and the Intensive Care Unit (ICU) departments and explained the study. Head nurses were informed to call the PI when there is admission with an AMI diagnosis. The PI met each participant, and the study was explained to the patient and their family members. If the participant agreed to participate in the study, a consent form was signed, including permission to review the medical record. When the participant was hemodynamically stable (MAP≥70 mm Hg) and within 72 hours (mean [SD], 42 [19] hours) of admission and per their preference, an interview was conducted to answer the sociodemographic questionnaire including necessary basic information of age, gender, marital status, severity and duration of chest pain. All other data were obtained from the medical records after participants were discharged.

It is worthy to note that the data collection was done during the COVID-19 pandemic. As well-trained personnel in academia, research, and clinical, PI used all protective measures and collaborated with the healthcare team during this period. The PI followed all necessary protocols announced by the government and the hospitals. Moreover, the PI has a 24-hours permit to go in and out, even during COVID 19 quarantine issued by the government.

2.4. Measurement of Variables

2.4.1. Clinical and Sociodemographic Characteristics

These information were collected either during patients interview or through medical records review after discharge: age, gender, marital status, smoking status, vital signs, the severity of chest pain on (a zero to ten scale), duration of chest pain in minutes, history of previous AMI, previous CABG, HTN, angina, DM, and stent use. Medications given in ED including Morphine, beta-blockers, thrombolytics, and any other analgesics. Moreover, the dose of Morphine in the ED was recorded in milligrams, then the use of Morphine was coded as either zero indicating 'no use' or one indicating 'use.' Morphine use in ICU was not recorded since most of the complications mentioned above usually occur in the ED or the first 24-72 hours after the event [19, 20].

2.4.2. In-Hospital Complications

In-hospital complications were determined by the presence of any of the following during the period of hospitalization after admission: (i) re-infarction; (ii) acute recurrent ischemia; (iii) ventricular fibrillation; (iv) sustained ventricular tachycardia (> 15 seconds), or any ventricular tachycardia requiring pharmacological and/or electrical intervention; (v) supra-ventricular tachyarrhythmia with hemodynamic instability; (vi) in-hospital death; (vii) acute pulmonary edema and (viii) cardiogenic shock [8, 19, 20]. These complications

were recorded after morphine administration and pain measurement till the patient was discharged. The total number of complications was recorded for hypothesis one testing. In addition, the development of complication was recoded as one indicating "occurred" and zero "did not occur" for hypotheses two and three testings.

2.5. Statistical Analysis

Data were analyzed using the Statistical Package for Social Science (SPSS version 25.0 for Windows). The statistical significance was considered at $\alpha < 0.05$. Descriptive statistics were used to describe and summarise all demographic and clinical variables. Mean, standard deviation, and range were used to describe the continuous variables. Frequency and percentage were used to describe the nominal variables. Additionally, the incidence was calculated for the following complications: acute recurrent ischemia, re-infarction incidence, supraventricular tachycardia incidence, sustained ventricular tachycardia, ventricular fibrillation, and ventricular tachycardia, cardiogenic shock, pulmonary edema, and in-hospital death.

2.5.1. Hypothesis One

One-way ANOVA with post hoc analysis was conducted to explore the impact of the chest pain severity on the number of complications developed after AMI.

2.5.2. Hypothesis Two

To test this hypothesis, two steps were done—step one: bivariate correlation between sociodemographic and clinical characteristics with complications. Person's r was used for continuous variables and Spearman's rho for categorical variables. The correlation was considered statistically significant in this step alone if p was <0.01. This was done to be more conservative in the prediction. Step two: all variables that significantly correlate with complications were included in a logistic regression model.

2.5.3. Hypothesis Three

The same process (step one and two) was done as in hypothesis two. In addition, an independent t-test was performed to compare the mean number of complications between those who received and did not receive Morphine. Furthermore, a chi-square test was performed to compare the number of patients who developed complications between those who received and those who did not receive Morphine.

3. RESULTS

3.1. Sociodemographic and Characteristics of the Sample

This study was conducted at the ED & ICU departments of four hospitals representing the four sectors of the healthcare system in Jordan. Three hundred participants participated in the study, including 176 (58.70%) men and 124 (41.30%) women with a mean age of 56.92±12.13 years (range of 33-88 years). Approximately two-thirds of the participants were hypertensive, and one-third had a history of previous angina. Additionally, more than a quarter of the sample had previous MI, and nearly half of the participants had a history of DM. Regarding the treatment with Morphine, 118 (39.3%) patients received Morphine, (Table **1**).

Table 1. Sociodemographic and clinical characteristics of the sample (N=300).

Characteristics	M±SD or n (%)
Age	56.92±12.13
Gender Male Female	176 (58.70) 124 (41.30)
Hospital Sector RMS Private Governmental Teaching	45 (15.0) 104 (34.7) 99 (33.0) 52 (17.3)
Marital status Single Married Divorced Widowed	20 (6.7) 256 (85.3) 10 (3.3) 14 (4.7)
Smoker	162 (54.0)
Previous angina	112 (37.3)
Previous MI	125 (41.7)
History of HTN	184 (61.3)
History of DM	156 (52.0)
Previous CABG	241 (80.3)
Stent Use	81 (27.0)
Received morphine	118 (39.3)
Dose of Morphine	3.81±1.15
Chest pain severity	5.22±2.26

(Table 1) contd.....

Characteristics	M±SD or n (%)
Duration of chest pain	5.54±3.57
Chest pain level	
Mild	93 (31)
Moderate	105 (35)
Severe	102 (34)

M: Mean. SD: Standard Deviation. N: Number. HTN: Hypertension. DM: Diabetes Mellitus. RMS: Royal Medical Services. MI: Myocardial Infarction. CABG: Coronary Artery Bypass Graft.

A description of specific complications developed by patients is presented in (Table **2**). A total of 83 (27.7%) patients developed a minimum one complication throughout hospitalization. The most common complications were: acute recurrent ischemia 70 (23.3%) patients; supra ventricular tachycardia 14 (4.7%); re-infarction 8 (2.7%), respectively.

Table 2. Specific complications developed with their percentages. (N=300).

Complication developed	*Number of patients (%)
Acute recurrent ischemia One time Two times Three times	70 (23.3) 40 (13.3) 22 (7.3) 8 (2.7)
SVT	14 (4.7)
Re-infarction	8 (2.7)
VT	5 (1.7)
Pulmonary edema	5 (1.7)
Cardiogenic shock	5 (1.7)
In-hospital death	5 (1.7)
Total complications in hospital	**83 (27.7)**

*More than one patient developed at least one complication. N: Number. SVT: supra-ventricular tachycardia: VT: ventricular tachycardia

3.2. Research Hypotheses

3.2.1. Research Hypothesis One

ANOVA was used to explore the impact of the chest pain severity on the number of complications developed after AMI. Chest pain severity was divided into three levels according to pain scales (mild (one-three), moderate (four-six), and severe (seven-ten). There was a statistically significant difference in the number of complications according to the levels of chest pain (pain severity) ($F_{(2,297)} = 4.713$, $p < .01$).

To identify which pain level was responsible for the significant main effect, post-hoc comparisons using the LDS test were made. Post hoc analyses showed that participants with severe chest pain had a higher complication rate than patients with mild chest pain. Moreover, patients with moderate chest pain had a higher complication rate than mild chest pain. However, there was no significant difference between severe and moderate chest pain groups (Table **3**).

3.2.2. Research Hypothesis Two

After controlling for socio-demographics and clinical characteristics, pain scores will be independent predictors for complications after AMI. Two steps were taken to test this hypothesis as mentioned previously. The significant variables entered into the binary logistic regression models were (pain severity, pain duration, previous angina and MI, history of HTN, aspirin use, and beta-blockers). The results of the regression model are shown in Table **4**. Among these variables, pain duration and severity were significant predictors. Chest pain duration of more than five minutes augmented the incidence of complications by 7%. In addition, severe pain ≥7 increased the incidence of complications by 13%. Furthermore, patients with previous MI and history of HTN were at higher risk of developing complications by 63% and 25%.

Table 3. LDS Post-hoc test of the number of complications among the levels of chest pain severity.

Chest pain levels	Compared with	Mean difference	*P*-value
Severe	Mild	.58	<0.01
	Moderate	.13	NS
Moderate	Mild	.45	<0.05

NS: Not significant.

Table 4. Predictors of in-hospital complications by Logistic regression/ Hypothesis two testing (N = 300).

Predictors	OR	CI	B	Wald	P-value
Chest Pain severity	1.13	1.06-1.27	0.12	3.93	0.04

(Table 4) contd.....

Predictors	OR	CI	B	Wald	P-value
Use of aspirin in-ED	1.30	0.77-2.19	0.26	0.98	0.32
Use of BB in-ED	1.06	0.61-1.84	0.05	0.04	0.84
Previous Angina	1.46	0.89-4.61	0.04	0.44	0.68
Previous MI	1.63	1.77-4.19	0.07	6.98	0.04
History of HTN	1.25	1.07-3.73	0.09	4.18	0.04
Chest pain duration	1.07	1.01-1.15	0.16	3.33	0.04

OR: Odds Ratio. CI: 95% Confidence Interval. B: Beta. ED: Emergency Department. MI: Myocardial infarction. HTN: Hypertension. BB: Beta-Blocker. DM: Diabetes Mellitus. CABG: Coronary Artery Bypass Graft.

Table 5. Predictors of in-hospital complications by Logistic regression/ Hypothesis three testing (N = 300).

Predictors	OR	CI	B	Wald	P-value
Chest Pain severity	1.14	1.06-1.29	0.12	3.97	0.04
Use of aspirin in-ED	1.28	0.76-2.22	0.27	.98	0.34
Use of BB in-ED	1.06	0.61-1.81	0.05	0.04	0.84
Use of Morphine in ED	1.02	0.57-1.64	0.04	0.04	0.76
Previous Angina	1.49	0.91-4.72	0.05	0.46	0.63
Previous MI	1.65	1.90-4.43	0.08	7.10	0.02
History of HTN	1.28	1.09-3.83	0.08	6.176	0.03
Chest pain duration	1.09	1.04-1.21	0.16	3.33	0.04

OR: Odds Ratio. CI: 95% Confidence Interval. B: Beta. ED: Emergency Department. MI: Myocardial infarction. HTN: Hypertension. BB: Beta-Blocker. DM: Diabetes Mellitus. CABG: Coronary Artery Bypass Graft.

3.2.3. Research Hypothesis Three

After controlling for socio-demographics and clinical characteristics, morphine use will be an independent predictor for complications after AMI. The exact process was done as in hypothesis two. The significant variables entered into the binary logistic regression models were (pain severity, pain duration, previous angina and MI, history of HTN, aspirin use, beta-blocker use, and Morphine use). The results of the regression model are shown in (Table **5**). As in hypothesis 2, chest pain severity, duration of chest pain more than 5 minutes, history of previous MI, and history of HTN were independent predictors for the occurrence of complications. However, morphine use was not a significant predictor. For further confirmation regarding this result, an independent t-test was done to compare the mean number of complications among those who received and did not receive Morphine. Again, the results showed no significant difference. Moreover, a chi-square test was done to check if the number of patients who developed complications differs between those who received and did not receive Morphine. Again, the results showed no significant difference between the two groups.

4. DISCUSSION

In the current study, it was found that higher levels of chest pain were linked with a higher incidence of complications. These results are consistent with other studies [8, 9]. Thus, this study affords additional support that chest pain plays a crucial role in increasing vulnerability to complications associated with AMI. In the current study, pain scores were independent predictors for the increased incidence of complications after AMI even after controlling for all other significant covariates determined in the literature. This supports a previous study done in Jordan [8]. Furthermore, patients with severe chest pain were at nearly five times greater risk of evolving complications than others [9]. Finally, it is worthy to note that there was a dose-response relationship between the severity of chest pain and the occurrence of complications in both studies.

The current study also found that the duration of chest pain was an independent predictor of complications. This finding is nearly the exact outcome of a previous study conducted on 426 patients diagnosed with AMI in the ED of Henry Ford Hospital in the United States, aiming to evaluate the association between the extent of chest pain and the diagnosis of AMI [9]. The study concluded that patients with short duration chest pain (less than five minutes) had a better prognosis than patients with chest pain duration of more than five minutes. In addition, the current study showed that patients who have chest pain duration of more than five minutes were at higher risk of developing complications after AMI than other patients (chest pain duration less than five minutes). Since complications are usually associated with a longer length of stay and poor prognosis, it is suspected that those who developed fewer complications will have a better prognosis.

Contrary, on a large sample of hospitalized patients with AMI, Björck *et al*. (2018) found that patients with no chest pain were more prone to develop not only higher rates of in-hospital mortality but also higher rates of long-term mortality over five years. These differences might be due to the delay in seeking help among asymptomatic patients. Several studies showed that a longer delay duration in seeking help was associated with more complications after AMI [21, 22] since the management of AMI is most effective within the first four hours after the occurrence of the event [22].

Historically, Morphine is considered one of the best treatments for chest pain in patients with AMI [23]. This treatment also included other therapeutics, such as oxygen, nitrates, and aspirin [7, 10, 13]. Morphine is given to patients

with AMI for different reasons: (1) it is considered a narcotic analgesic that relieves pain; (2) it helps in decreasing the level of anxiety; and lastly, (3) morphine dilates the peripheral vascular system [24] and therefore, it decreases the systemic vascular resistance and the workload of the heart.

Despite these advantages, there are undesirable side effects that healthcare team should be aware of when using Morphine. These include but are not limited to: hypotension, nausea, vomiting, and respiratory depression. These side effects might be worse than the chest pain itself for some patients, and might enhance the occurrence of complications after AMI, especially hypotension, since it decreases the coronary blood flow and coronary blood supply.

The current study investigated whether morphine administration early after the event would have a protective effect on the occurrence of complications. The results indicated that morphine administration did not have any protective effect against these complications. Previous literature on the relationship between Morphine and complications after AMI concluded one of three outcomes: First: The use of Morphine did not have any protective effect against these complications [12, 25 - 27]. Second: The use of Morphine did not have any adverse impact on the complications after AMI [26, 27]. Third: The use of Morphine resulted in more complications, including suboptimal reperfusion of coronary arteries, a larger infarct size [7, 28], and a higher mortality rate [16].

First: Morphine administration did not have any protective effect against these complications. This result was concluded by a study similar to the current study [8] on 371 patients with AMI. However, the previous study used a retrospective design, and it included a relatively small number of patients who received Morphine (n = 71, 19.1%) with doses ranging from 2.5-5 mg. Alternatively, in the present study (n = 118, 39.3%) patients received Morphine from 1-4 mg, which is relatively higher. It is worthy to note that the recommended dose for morphine post-AMI based on ESC, AHA, and ACC is from 4-8 mg [6, 10, 13]. This might explain why those patients who received Morphine did not have any protective effect in the current study. However, in the previous study, the dose of Morphine was within the recommended dose, and despite that, the same results were found.

A double-blind RCT [25] was conducted on 91 patients with STEMI to identify the possible cardio-protective effect of intracoronary 1 mg morphine vs. placebo administration. The authors concluded that administration of Morphine through intracoronary had no impact on improving the contraction ability of the left ventricle or dropping the infarct size in those patients with STEMI. These results are nearly the same as the results of the current study.

Second: Two studies [26, 27] showed that morphine use did not negatively affect the outcomes after AMI. The first was a descriptive correlational study on 1,726 patients with STEMI, checking the relation between morphine administration in the pre-hospital period and clinical outcomes of those patients with STEMI. The results showed that the administration of Morphine before hospital admission was not linked with worse in-hospital complications and one-year survival.

The second study [26] was conducted in Korea on 299 patients with STEMI who were undergoing primary Percutaneous Intervention (PCI) to determine whether the use of Morphine harms myocardial injury. The primary conclusion was that using morphine proceeding to primary PCI among STEMI patients did not raise the amount of myocardial impairment or cause contrary outcomes in the myocardial retrieve.

Third: In contrast to the results of the current study, three previous studies [7, 16, 28] reported adverse effects of morphine use. In these studies, the use of Morphine resulted in more complications, including suboptimal reperfusion of coronary arteries, a larger infarct size [7, 28], and a higher mortality rate [16]. The explanation of the differences in these results might be due to one or more of the following: (1) interactions between Morphine, and P2Y12 receptor-inhibitors impede their action, leading to reduced gastrointestinal absorption, the diminished concentration of energetic metabolites, and deferred antiplatelet activity, (2) drug-drug interaction and different statistical methods used (non-randomized) to avoid selection bias in the observational study, (3) morphine administration masks the symptoms than treating the cause.

CONCLUSION AND IMPLICATION TO NURSING PRACTICE

This study showed that the severity and the duration of chest pain increased the occurrence of in-hospital complications after AMI. The administration of Morphine did not have any protective effect against the incidence of these complications. Chest pain typically results from the inequality between oxygen supply and request. Accordingly, nurses as front-line healthcare team dealing with those patients can suggest that other chest pain-relief approaches, including treating the underlying cause of chest pain and addressing the imbalance between oxygen supply and demand, should be assimilated into the treatment protocols and policies. Furthermore, it is highly recommended that nurse practitioners and researchers, along with a multidisciplinary healthcare team, conduct RCT to determine the effect of Morphine on complications after AMI

LIST OF ABBREVIATIONS

AMI	=	Acute Myocardial Infarction
ICU	=	Intensive Care Unit
MF	=	Myocardial Infarction
ED	=	Emergency Department

AUTHORS' CONTRIBUTIONS

All authors contributed significantly to work reported, including the conception, study design, execution, acquisition of data, analysis and interpretation, draft writing, and substantially revised and critically reviewed the article.

LIMITATIONS

The major limitation of this study was the use of the medical records for some of the data collection, which depends

on the documentation from other people. Additionally, the exclusion of hemodynamically unstable patients was a significant limitation of this study, which might decrease the incidence of in-hospital complications.

ETHICAL STATEMENT

This study was approved from the IRB committees from all cites before data collection stated (IRB#: Faculty 2019-2020-4-4).

CONSENT FOR PUBLICATION

Informed consent has been obtained from all participants.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIAL

Not applicable.

FUNDING

None

CONFLICT OF INTEREST

All authors declare no conflict of interest in this work.

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Declared none.

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