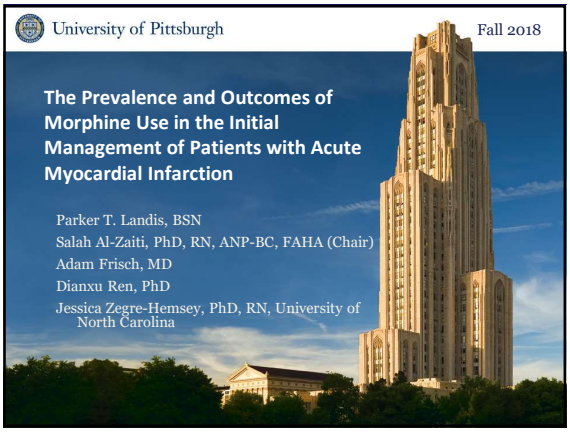
University of Pittsburgh Fall 2018

The Prevalence and Outcomes of Morphine Use in the Initial Management of Patients with Acute Myocardial Infarction

Parker T. Landis, BSN
Salah Al-Zaiti, PhD, RN, ANP-BC, FAHA (Chair)
Adam Frisch, MD
Dianxu Ren, PhD
Jessica Zegre-Hemsey, PhD, RN, University of North Carolina



University of Pittsburgh

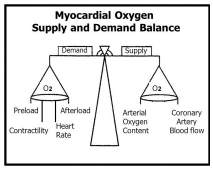
Overview

1. Background
2. Purpose and Aims
3. Design
4. Results
5. Clinical Implication
6. Conclusion

University of Pittsburgh

M.O.N.A.

- **Morphine** - Severe chest pain unrelieved by nitroglycerin
- **Oxygen** - Hypoxemia (SpO2<90%)
- **Nitroglycerin** - Hypertension or LVHF
- **Aspirin** - Anticoagulation



University of Pittsburgh

Applying Classification of Recommendation and Level of Evidence

Size of Treatment Effect

Estimate of Certainty (Precision) of Treatment Effect

	Class I Benefit >>>Risk Treatment should be administered	Class IIa Benefit >> Risk It is reasonable to administer treatment	Class IIb Benefit ≥ Risk Treatment may be considered	Class III No benefit or harm
Level A Multiple populations evaluated	MONA			
Level B Limited populations evaluated			MONA NSTEMI	
Level C Very limited population evaluated	MONA	MONA STEMI		

University of Pittsburgh

History of Guidelines

ACC/AHA Guidelines	Class of Recommendation	Level of Evidence
1999 Acute MI	I	-
2004 STEMI	I	C
2007 NSTEMI	IIa	B
2013 STEMI*	-	-
2014 NSTEMI*	**IIb**	**B**

ESC Guidelines	Class of Recommendation	Level of Evidence
2002 Chest Pain	I	C
2012 STEMI	I	C
2015 NSTEMI*	-	-
2017 STEMI*	**IIa**	**C**

* Most recent guidelines

University of Pittsburgh

Literature- Morphine Showed Adverse Outcomes

YEAR	STUDY DESIGN	POPULATION	INTERVENTION	CLINICAL OUTCOME
2005	Nonrandomized, retrospective, observational registry	n=57,039 NSTEMI patients	Acute morphine administration (<24hrs)	Morphine was associated with higher mortality
2017	Nonrandomized, retrospective study	n=3,027 AMI patients	Morphine prior to PPCI	NSTEMI- larger infarct size & longer LOS STEMI- no affect on outcomes

University of Pittsburgh

Literature- Morphine Did Not Show Adverse Outcomes

YEAR	STUDY DESIGN	POPULATION	INTERVENTION	CLINICAL OUTCOME
2015	Nonrandomized, secondary analysis of RCT dataset	n=276 STEMI patients	Morphine administration within 10hrs pre-PCI	No observed association of IV morphine on MACE or mortality
2016	Nonrandomized, observational study	n=182 anticoagulant naïve STEMI patients	Morphine administration pre-PCI	Morphine was not associated with MACE
2016	Nonrandomized, retrospective, cohort study	n=2,438 STEMI patients	Prehospital morphine administration	Morphine was not associated with worse in-hospital or 1-year complications
2017	Nonrandomized, secondary analysis retrospective study	n=969 STEMI patients	Morphine prior to PPCI	Morphine was not associated with 1-year MACE
2018	Nonrandomized, prospective study	n=300 STEMI patients	Morphine prior to PPCI	Morphine was not associated with MACE

University of Pittsburgh

Purpose

The purpose of this study is to evaluate the safety and efficacy of intravenous morphine use in AMI patients.

- Population - AMI patients
- Intervention - Intravenous morphine
- Comparison - No intravenous morphine
- Outcome – Clinical outcomes

University of Pittsburgh

Theoretical Framework

- Anticoagulation is a vital intervention in AMI morbidity and mortality.
- Dual Antiplatelet Therapy (DAPT) is indicated in PCI
  - $P2Y_{12}$ inhibitor and aspirin loading doses
- Morphine is shown to decrease oral $P2Y_{12}$ inhibitor concentrations and effects in AMI patients.

University of Pittsburgh

Specific Aim 1 - Determine the prevalence of morphine administration

- Aim 1(a). What is the prevalence of morphine administration among AMI patients? STEMI? NSTEMI?
- Aim 1(b). Are there demographical and clinical differences between patients who were or were not administered morphine?

University of Pittsburgh

Specific Aim 2 - Evaluate the relationship between morphine administration and clinical outcomes

- Aim 2(a). Is there a relationship between morphine use and size of infarct in STEMI vs. NSTEMI patients after controlling for potential confounders?
- Aim 2(b). Is there a relationship between morphine use and myocardial dysfunction in STEMI vs. NSTEMI patients after controlling for potential confounders?
- Aim 2(c). Is there a relationship between morphine use and 30-day MACE in STEMI vs. NSTEMI patients after controlling for potential confounders?

University of Pittsburgh

Design & Setting

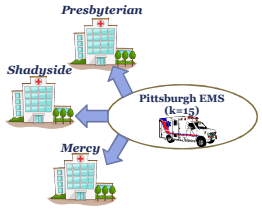
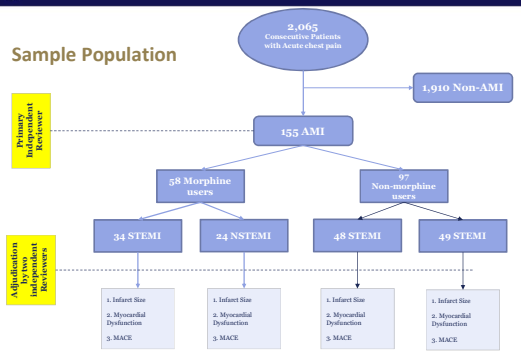


Figure 10: Flowchart of Study Design

Secondary analysis of EMPIRE (*Electrocardiographic Methods for the Prompt Identification of Coronary Events*)

University of Pittsburgh

Sample Population



University of Pittsburgh

Variables

- **Baseline Variables**
  - Demographics, PMH
  - Admission time/date, length of stay
  - Morphine dose/time, Oxygen, Nitroglycerin and Pre-procedural aspirin administration at the ED
  - First three consecutive troponin blood values/time
  - Lesion type
- **Independent Variable**: IV morphine
- **Dependent Variable**: Infarct size, Myocardial Dysfunction, MACE

University of Pittsburgh

Primary Outcomes

1. **Infarct size** - defined by peak troponin level
2. **Myocardial dysfunction** - defined by left ventricular ejection fraction
3. **MACE** - defined as all-cause death, fatal ventricular arrhythmia, acute heart failure, pulmonary edema, cardiogenic shock, re-infarction, or repeat catheterization within 30 days of indexed admission

University of Pittsburgh

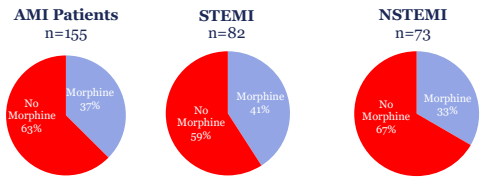
Statistical Analysis

- **Descriptive**
  - Means ± SD, Median [25th – 75th percentiles], n (%)
- **Compare Groups** (morphine users vs. non-users)
  - t-test, chi-square
- **Evaluate Predictors**
  - Linear or Logistic regression

University of Pittsburgh

Results

Aim 1(a). Prevalence of morphine administration among AMI patients? STEMI? NSTEMI?



University of Pittsburgh

Aim 1(b). Demographical and clinical differences between patients who were or were not administered morphine?

Demographics	Morphine users (n=58)	Non-Morphine users (n=96)	P-Value
Age (years)±SD	61±18	66±14	**0.030***
BMI (kg/m2)±SD	31.2±8.5	29.6±6.8	0.190
Male	60%	58%	0.730
Black	36%	25%	0.148
Smoker	67%	57%	0.461
Medical History	**Morphine users (n=58)**	**Non-Morphine users (n=96)**	**P-Value**
HTN	74%	70%	0.587
DM2	35%	31%	0.724
HLD	50%	54%	0.622
HF	19%	12%	0.237
CAD	45%	38%	0.400
Angina	19%	9.40%	0.136
Prior MI	28%	28%	0.940
PAD	9%	6%	0.748
Prior Stroke	8.50%	10.40%	0.339
Chronic Lung Disease	28%	21%	0.432
Prior PCI	29%	25%	0.577
Prior CABG	14%	14%	0.965

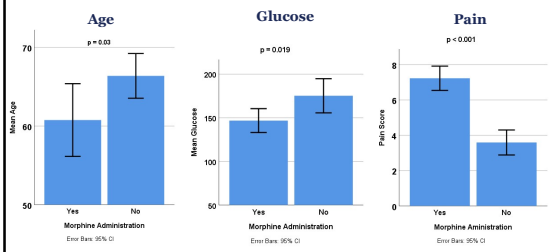
University of Pittsburgh

Aim 1(b). Demographical and clinical differences between patients who were or were not administered morphine?

Vessel Occlusion	Morphine users (n=58)	Non-Morphine users (n=96)	P-Value
LAD (%)±SD	81±21	75±27	0.269
LCx (%)±SD	68±28	66±27	0.743
RCA (%)±SD	75±30	76±30	0.905
Culprit Lesion			
LAD	41%	49%	0.406
LCx	19%	23%	0.686
RCA	36%	36%	0.975
Presenting Signs	**Morphine users (n=58)**	**Non-Morphine users (n=96)**	**P-Value**
Cr median(25th-75th percentile)	1.0[0.8-1.2]	1.0[0.9-1.3]	0.175
Glucose (mg/dL)±SD	147±51	175±95	**0.019***
SOB	59%	52%	0.505
Diaphoresis	40%	46%	0.504
GI Upset	43%	47%	0.496
PH HR (beat/min)±SD	86±20	84±31	0.730
PH RR (Respirations/min)±SD	20±4	19±4	0.180
PH SaO2 (%)±SD	98±3	98±3	0.510
PH SBP (mmHg)±SD	144±36	146±43	0.830
PH DBP (mmHg)±SD	86±27	86±22	0.900
Pain (0-10)±SD	7.4±2.6	3.9±3.5	**<0.001***

University of Pittsburgh

Aim 1(b). Demographical and clinical differences between patients who were or were not administered morphine?



University of Pittsburgh

Aim 2(a). Is there a relationship between morphine use and size of infarct in STEMI vs. NSTEMI patients after controlling for potential confounders?

Univariate and Multivariate Predictors of Infarct Size

	STEMI		NSTEMI	
Predictors	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**
Demographics				
Age	NS	–	NS	–
Sex	NS	–	NS	–
Race	NS	–	NS	–
BMI	NS	–	NS	–
Smoking	NS	–	NS	–
Past Medical History				
HTN	NS	–	p = 0.080	**p = 0.037**
DM	NS	–	NS	–
Dyslipidemia	NS	–	NS	–
Known HF	NS	–	NS	–
CAD	NS	–	NS	–
Angina	NS	–	NS	–
Prior MI	NS	–	NS	–
PAD	NS	–	NS	–
Prior Stroke	NS	–	NS	–
Chronic Lung Disease	NS	–	NS	–
Prior PCI	NS	–	NS	–
Prior CABG	NS	–	NS	–

University of Pittsburgh

Aim 2(a). Is there a relationship between morphine use and size of infarct in STEMI vs. NSTEMI patients after controlling for potential confounders?

	STEMI		NSTEMI	
Predictors	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**
Clinical Presentation				
SOB	NS	–	NS	–
Diaphoresis	NS	–	NS	–
GI Upset	NS	–	NS	–
HR	NS	–	p = 0.049	p = 0.073
RR	NS	–	p = 0.034	**p = 0.048**
SBP	NS	–	NS	–
DBP	NS	–	NS	–
O2 Sat	NS	–	NS	–
Pain Score	NS	–	0.073	p = 0.284
Diagnostic Workup				
Glucose	NS	–	NS	–
Creatinine	NS	–	NS	–
LAD Occlusion	NS	–	NS	–
LCX Occlusion	NS	–	NS	–
RCA Occlusion	NS	–	NS	–
Initial Treatment				
Oxygen at the ED	NS	–	p = 0.002	**p = 0.002**
IV Morphine	NS	–	p = 0.086	p = 0.133

University of Pittsburgh

Aim 2(b). Is there a relationship between morphine use and myocardial dysfunction in STEMI vs. NSTEMI patients after controlling for confounders?

	STEMI		NSTEMI	
Predictors	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**
Demographics				
Age	NS	–	NS	–
Sex	p = 0.016	**p = 0.044**	NS	–
Race	NS	–	NS	–
BMI	NS	–	NS	–
Smoking	NS	–	NS	–
Past Medical History				
HTN	NS	–	NS	–
DM	NS	–	NS	–
Dyslipidemia	NS	–	p = 0.060	p = 0.084
Known HF	p = 0.013	**p = 0.014**	p = 0.052	p = 0.361
CAD	NS	–	NS	–
Angina	NS	–	NS	–
Prior MI	NS	–	NS	–
PAD	p = 0.071	p = 0.393	NS	–
Prior Stroke	NS	–	NS	–
Chronic Lung Disease	NS	–	NS	–
Prior PCI	NS	–	NS	–
Prior CABG	NS	–	NS	–

University of Pittsburgh

Aim 2(b). Is there a relationship between morphine use and myocardial dysfunction in STEMI vs. NSTEMI patients after controlling for confounders?

	STEMI		NSTEMI	
Predictors	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**
Clinical Presentation				
SOB	NS	–	p = 0.023	**p = 0.049**
Diaphoresis	NS	–	NS	–
GI Upset	NS	–	NS	–
HR	NS	–	NS	–
RR	NS	–	NS	–
SBP	NS	–	NS	–
DBP	NS	–	NS	–
O2 Sat	NS	–	NS	–
Pain Score	NS	–	NS	–
Diagnostic Workup				
Glucose	NS	–	NS	–
Creatinine	NS	–	NS	–
LAD Occlusion	p = 0.001	**p = 0.002**	NS	–
LCX Occlusion	NS	–	NS	–
RCA Occlusion	NS	–	NS	–
Initial Treatment				
Oxygen at the ED	NS	–	NS	–
IV Morphine	NS	–	p = 0.046	p = 0.084

University of Pittsburgh

Aim 2(c). Is there a relationship between morphine use and 30-day MACE in STEMI vs. NSTEMI patients after controlling for potential confounders?

	STEMI (n=82)		NSTEMI (n=71)	
Predictors	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**
Demographics				
Age	NS	–	NS	–
Sex	NS	–	NS	–
Race	NS	–	NS	–
BMI	NS	–	NS	–
Smoking	NS	–	NS	–
Past Medical History				
HTN	NS	–	NS	–
DM	NS	–	NS	–
Dyslipidemia	NS	–	NS	–
Known HF	p = 0.034	p = 0.254	NS	–
CAD	NS	–	NS	–
Angina	NS	–	NS	–
Prior MI	NS	–	NS	–
PAD	NS	–	NS	–
Prior Stroke	NS	–	NS	–
Chronic Lung Disease	NS	–	NS	–
Prior PCI	NS	–	NS	–
Prior CABG	NS	–	p = 0.075	**p = 0.040**

University of Pittsburgh

Aim 2(c). Is there a relationship between morphine use and 30-day MACE in STEMI vs. NSTEMI patients after controlling for potential confounders?

	STEMI (n=82)		NSTEMI (n=71)	
Predictors	**Univariate**	**Multivariate**	**Univariate**	**Multivariate**
Clinical Presentation				
SOB	NS	–	p = 0.112	p = 0.125
Diaphoresis	NS	–	NS	–
GI Upset	NS	–	NS	–
HR	NS	–	NS	–
RR	NS	–	NS	–
SBP	p = 0.007	**p = 0.041**	NS	–
DBP	NS	–	NS	–
O2 Sat	NS	–	NS	–
Pain Score	NS	–	NS	–
Diagnostic Workup				
Glucose	p = 0.016	p = 0.143	p = 0.051	**p = 0.029**
Creatinine	p = 0.011	**p = 0.017**	NS	–
LAD Occlusion	NS	–	NS	–
LCX Occlusion	NS	–	NS	–
RCA Occlusion	NS	–	NS	–
Initial Treatment				
Oxygen at the ED	NS	–	NS	–
IV Morphine	NS	–	NS	–

University of Pittsburgh

Summary of Results

	STEMI	NSTEMI
Infarct Size	-	HTN (p=0.037)
	-	RR (p=0.048)
	-	O2 administered at the ED (p=0.002)
Myocardial Dysfunction	Sex (p=0.044)	SOB (p=0.049)
	known heart failure (p=0.014)	-
	LAD occlusion (p=0.002)	-
MACE	SBP (p=0.041)	Prior CABG (p=0.040)
	Cr (p=0.017)	glucose (0.029)

University of Pittsburgh

Discussion - STEMI

- Our results are congruent with literature providing evidence that clinical outcomes are unaffected by morphine
- There is no evidence contradicting use of morphine in STEMI patients

University of Pittsburgh

Discussion - NSTEMI

- Literature is controversial regarding morphine use in NSTEMI
  - Some studies show links to adverse outcomes
- Our data showed trends toward increased myocardial dysfunction and infarct size in NSTEMI
  - Unclear if misk may exceed benefit in NSTEMI
  - Our study was one of few that included MACE

University of Pittsburgh

Conclusion

- In this study, morphine use was not associated with infarct size, myocardial dysfunction, or MACE after controlling for MI type and other potential confounders.


University of Pittsburgh
Thank You