Patient characteristics and outcomes of acute myocardial infarction presenting without ischemic pain: Insights from the Atherosclerosis Risk in Communities Study

Bailey M. DeBarmore[a,*], **Jessica K. Zègre-Hemsey**[b], **Anna M. Kucharska-Newton**[a,c], **Erin D. Michos**[d,e], **Wayne D. Rosamond**[a]

[a]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

[b]School of Nursing, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

[c]Department of Epidemiology, College of Public Health, University of Kentucky, Lexington, KY, USA

[d]Ciccarone Center for the Prevention of Cardiovascular Disease, Johns Hopkins School of Medicine, Baltimore, MD, USA

[e]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health Baltimore, MD, USA

Abstract

Background: Our objective was to describe characteristics of patients presenting with and without ischemic pain among those diagnosed with acute myocardial infarction (MI) using individual-level data from the Atherosclerosis Risk in Communities Study from 2005 to 2019.

Methods: Acute MI included events deemed definite or probable MI by a physician panel based on ischemic pain, cardiac biomarkers, and ECG evidence. Patient characteristics included age at hospitalization, sex, race/ethnicity, comorbidities (smoking status, diabetes, hypertension, history of previous stroke, MI, or cardiovascular procedure, and history of valvular disease or cardiomyopathy) and in-hospital complications occurring during the event of interest (pulmonary

---

*Corresponding author. Bailey.debarmore@gmail.com (B.M. DeBarmore).

edema, pulmonary embolism, in-hospital stroke, pneumonia, cardiogenic shock, ventricular fibrillation). Analyses were stratified by MI subtype (STEMI, NSTEMI, Unclassified) and patient characteristics and 28-day case fatality was compared between MI presenting with or without ischemic pain.

Results: Between 2005 and 2019, there were 1711 hospitalized definite/probable MI events (47 % female, 26 % black, and age of 78 [6.7 years]). A smaller proportion of STEMI patients presented without ischemic pain compared to NSTEMI patients (20 % vs 32 %). Race, sex, age, and comorbidity profiles did not differ significantly across ischemic pain presentations. Patients presenting without ischemic pain had a higher 28-day all-cause case fatality after adjusting for age, race, sex, and comorbidities. However, after further adjustment, time from symptom onset to hospital arrival, time to treatment, and in-hospital complications explained the difference in 28-day case fatality between ischemic pain presentations.

Conclusions: Future research should focus on differences in treatment delay across ischemic pain presentations rather than sex differences in acute coronary syndrome presentation.

1. Introduction

Chest pain and associated jaw, arm, and shoulder pain, are the most commonly recognized symptoms of acute myocardial infarction (MI). However, MI presentation with other symptoms is well-documented, particularly within treatment guidelines that highlight differences in MI symptom presentation by sex [1]. Specifically, not all acute MI patients present with pain or discomfort in the chest, left shoulder, arm, or jaw. These classic symptoms of MI are often referred to as "typical MI" in contrast to other ischemic presentations including shortness of breath, nausea/indigestion, extreme fatigue, back discomfort, etc., that are often referred to "atypical" [2]. Ischemic pain symptoms should be further distinguished from non-cardiac chest pain, such as pain arising from a musculoskeletal or gastro-intestinal etiology, which are also commonly labeled as "atypical" but reflect non-ischemic diagnoses (i.e., no MI) [3,4]. In October 2021, the American Heart Association (AHA) and the American College of Cardiology (ACC) issued a joint statement on clinical practice guidelines for evaluation and diagnosis of chest pain. Among the 10 take-home messages was to replace the use of "atypical" chest pain and symptoms with "noncardiac", as the term "atypical" is a "misleading descriptor of chest pain and its use is discouraged" [2].

Patients experiencing an acute MI event *without* ischemic pain symptoms are more likely to experience delayed hospital arrival [5–7], have a lower likelihood of receiving medical therapies and cardiac procedures [8], and experience higher mortality compared to patients presenting *with* ischemic pain symptoms [9,10]. Previous literature reports older age, female sex, black race, and diabetes as associated with presentation without ischemic pain symptoms [10–14], but patient characteristics and case fatality among patients presenting without ischemic pain have not been described in a large community-based prospective

study. Further characterization of the occurrence of acute MI without ischemic pain may inform triage and risk stratification for this class of events. Present analyses, using cohort surveillance data collected from 2005 through 2019 as part of the Atherosclerosis Risk in Communities (ARIC) Study, compare age-standardized patient characteristics, including sex, race, comorbidities, and in-hospital complications, and 28-day case fatality among hospitalized MI events stratified by STEMI/NSTEMI and ischemic pain presentation.

2. Methods

2.1. Study population

The ARIC Study is an ongoing prospective cohort study of 15,792 individuals aged 45–64 initially recruited from 4 US communities (Forsyth County, North Carolina; Jackson, Mississippi; suburban Minneapolis, Minnesota; and Washington County, Maryland) between 1987 and 1989 [15]. Follow-up visits occurred in 1990–1992 (visit 2), 1993–1995 (visit 3), 1996–1998 (visit 4), 2011–2013 (visit 5), 2016–2017 (visit 6), 2018–2019 (visit 7), and 2020–2021 (visit 8) with annual or semi-annual telephone follow-up in between visits, during which participants are asked about hospitalizations. Cohort surveillance for hospitalized myocardial infarction (MI) began at the beginning of the study in 1987.

2.2. Hospitalized MI events and case fatality

Hospitalized events are identified via participant/proxy telephone interviews and review of hospital discharge indices from hospitals in the area of the four ARIC communities. During telephone interviews, participants or proxies are asked about hospitalizations at any location and medical charts for those hospitalizations are then requested. Hospitalization records and hospital discharge indices are reviewed for the presence of ICD-9-CM (402, 410–414, 427, 428, 518.4) and ICD-10-CM (I11, I20, I21, I22, I24, I25, I46, I47, I48, I49, I50, J81, R00.1) codes [16]. Medical records with these codes, or other codes where a review of the discharge summary suggests a cardiac event, are abstracted for presence of ischemic pain, history of MI or cardiovascular disease, and cardiac biomarkers (e.g., troponin). Copies of up to 3 electrocardiograms (ECG) (first, last, and third) are obtained from each hospitalization and classified according to the Minnesota coding system [17,18]. Each MI event is classified as definite, probable, suspect, or no MI based on the presence of ischemic pain, biomarker levels, and electrocardiographic data by a standardized computerized algorithm and then, for final classification, by 2 physicians on the ARIC Mortality and Morbidity Classification Committee, with disagreements resolved by the committee chair (Supplemental Fig. 2). Criteria for each of the 3 diagnostic algorithm elements have remained constant during the study period (2005 to 2019) and have been previously described in detail elsewhere [19]. Specifics of the ECG and biomarker criteria used are described in the Supplemental material.

For the present analyses, definite and probable MI events were combined and cases with equivocal or abnormal biomarkers were further classified as STEMI or NSTEMI according to the assigned ECG Minnesota code [17]. Time from symptom onset to hospital arrival and time from symptom onset to treatment were abstracted from the medical records. MI events that could not be classified as STEMI or NSTEMI were labeled as "unclassified".

Patients' vital status following MI hospitalization and discharge was determined through cohort fatality surveillance and linkage with National Death Index files. Twenty-eight day case-fatality was calculated as time from MI event to death [16].

2.3. Ischemic pain presentation

Possible ischemic pain in the 72 h prior to the acute MI event, or at the time of an in-hospital event, was categorized as present or absent. Trained medical record abstractors reviewed the full hospital medical record to record if a physician determined that the pain was of cardiac (i.e. ischemic chest pain) or non-cardiac origin. For the present analyses, patients with pain of cardiac origin were classified as MI "with ischemic pain", and those without pain or with pain of non-cardiac origin (e.g., gastrointestinal) were classified as MI "without ischemic pain" (Fig. 1). Thus, events classified as "MI *without* ischemic pain symptom presentation" include definite/probable MI events where patients presented either with no cardiac pain at all, or with cardiac-like pain *determined to be of non-cardiac origin*. For further details, please see the Supplemental Table 1 and Supplemental Fig. 2. Participants missing data on ischemic pain from the hospitalized MI event (n = 196) and all events occurring before 2005 were excluded in order to utilize troponin measurements for MI classification (n = 2164) (Supplemental Fig. 1).

2.4. Comorbidities and complications

Trained medical record abstractors identified comorbidities and in-hospital complications from the medical records. Comorbidities assessed in these analyses included smoking status (current, former, never), history of stroke, hypertension, history of percutaneous coronary intervention (PCI) or history of coronary artery bypass grafting (CABG) procedure, history of valvular disease or cardiomyopathy, history of ischemic heart disease, previous MI, and diabetes. In-hospital complications, occurring during the hospitalization for the MI event identified, included pulmonary edema, pulmonary embolism, in-hospital stroke, cardiogenic shock, pneumonia, and ventricular fibrillation.

2.5. Statistical analyses

We present patient characteristics, including sex, race, comorbidities, and in-hospital complications by ischemic pain presentation for all MI as well as by MI subtype (STEMI, NSTEMI, Unclassified) and pain presentation. Predicted margins are presented as adjusted predicted probabilities of comorbidities and in-hospital complications and were estimated from logistic regression adjusted for age and event year. The adjustment for the year of hospitalization was made to account for possible changes in management of MI and prevalence of risk factors over the analysis period. We estimated the adjusted 28-day all-cause case fatality from symptom onset using logistic regression and predicted margins, exploring several models of progressive variable adjustment. Model 1 estimated 28-day case fatality adjusted for age and event year. Model 2 adjusted for Model 1 plus sex and race. Model 3A adjusted for Model 2 plus comorbidities (diabetes, previous MI or ischemic heart disease, history of valvular disease or cardiomyopathy, previous CABG or PCI, history of stroke, hypertension) and smoking status (current, former, never). Model 3B adjusted for Model 2 plus time from symptoms to hospital arrival, time from symptoms to treatment (intravenous or intracoronary reperfusion, stent placement, atherectomy, percutaneous

coronary intervention [PCI], or coronary artery bypass grafting [CABG]), and occurrence of any in-hospital complications (pulmonary edema, pulmonary embolism, pneumonia, in-hospital stroke, cardiogenic shock, ventricular fibrillation). Model 4 adjusted for Model 2 variables plus comorbidities, smoking status, time from symptoms to hospital arrival, time from symptoms to treatment, and occurrence of any in-hospital complications. Data tables for figures are provided in the Supplemental content. Data was analyzed using Stata IC 16.1 (Copyright © 2019 StataCorp LP, College Station, TX, USA) and SAS software Version 9.4 for Windows (Copyright © 2017 SAS Institute Inc., Cary, NC, USA). The ARIC study has been approved by the institutional review boards of participating institutions and all participants provided written informed consent.

3. Results

3.1. Study population

Between 2005 and 2019, there were a total of 1711 hospitalized MI events classified as definite or probable MI and meeting our inclusion criteria. Of these, 124 (7 %) were classified as STEMI, 1260 (74 %) were classified as NSTEMI, and 327 (19 %) were not classified as either MI subtype (unclassified MI). Twenty percent of participants with STEMI events, 32 % of participants with NSTEMI events, and 37 % of participants with unclassified MI events presented without ischemic pain.

3.2. Patient characteristics

The average age among participants with hospitalized MI events was 78.3 years (SD 6.7 years) and similar across MI subtypes and ischemic pain presentations (Table 1). A larger proportion of participants presenting with STEMI without ischemic pain were black women (24 % vs 8 %) or black men (16 % vs 10 %) compared to participants presenting with STEMI with ischemic pain (Table 1); however, race and sex distributions were similar across ischemic pain presentation for NSTEMI and Unclassified MI (Table 1). Adjusted for age and event year did not change the distribution of race or sex across MI subtypes or ischemic pain presentation.

3.3. Comorbidities, complications, and survival

The proportion of patients with diabetes, previous MI or ischemic heart disease, hypertension, and previous stroke were similar between ischemic pain presentations for all MI subtypes, as was being a current smoker, even after adjusting for age and hospitalization year (Fig. 2, Supplemental Fig. 5). A history of valvular disease or cardiomyopathy was more common among participants with STEMI events without ischemic pain than with ischemic pain (32 % vs 11 %, p = 0.02, Fig. 2). Among participants presenting with NSTEMI, those without ischemic pain were less likely to have had a previous CABG or PCI than those with ischemic pain (38 % vs 46 %, p = 0.008, Fig. 2).

Hospital arrival within 2 h of symptom onset was less common in participants presenting without ischemic pain across all MI subtypes. Eighteen percent of STEMI participants with STEMI with ischemic pain had treatment within 2 h of symptom onset compared to 13 % of those without ischemic pain (p = 0.09, Fig. 3) [20]. Time to treatment among participants

with NSTEMI did not differ by ischemic pain presentation, with over 80 % receiving treatment >6 h after symptom onset (Fig. 3) [21].

The occurrence of any in-hospital complication was more common among participants presenting without ischemic pain than with ischemic pain across all MI subtypes (STEMI: 52 % vs 23 %, p = 0.008; NSTEMI: 59 % vs 37 %, p < 0.0001; Unclassified MI: 48 % vs 33 %, p = 0.005). Regarding specific complications, pulmonary edema and pneumonia were more common among STEMI without ischemic pain (32 % vs 13 %, p = 0.06 and 20 % vs 4 %, p = 0.08) and unclassified MI without ischemic pain (41 % vs 27 %, p = 0.01 and 19 % vs 6 %, p = 0.002) than with ischemic pain (Supplemental Fig. 5). In addition to pulmonary edema and pneumonia, in-hospital stroke (6 % vs 2 %, p = 0.002) and ventricular fibrillation (6 % vs 8 %, p = 0.0007) were more common among NSTEMI without ischemic pain than with ischemic pain (Supplemental Fig. 5).

Participants presenting with MI (across subtypes) without ischemic pain had a higher 28-day case fatality than those presenting with ischemic pain, independent of age, event year, race, sex, and comorbidities (Fig. 4, Model 3A). However, after additionally adjusting for time from symptom onset to hospital arrival, time from symptom onset to treatment, and occurrence of in-hospital complications, there was no significant difference between those presenting with and without ischemic pain (Fig. 4, Model 4).

4. Discussion

In contrast to existing studies [10–14,22], we observed that female sex, Black race, older age, and presence of diabetes was not associated with MI presentation without ischemic pain, regardless of MI subtype. We did find that participants presenting with MI without ischemic pain constitute a substantial proportion of both STEMI (20 %) and NSTEMI (32 %) patients and have worse outcomes associated with their MI event compared to those presenting with ischemic pain that could not be explained by age, race, sex, or comorbidities. The difference in 28-day case fatality by ischemic pain presentation could, however, be explained by longer time from symptom onset to hospital, long time from symptom onset to treatment, and occurrence of in-hospital complications. These findings are consistent with existing research reporting increased in-hospital and 30-day mortality among patients presenting without ischemic pain [10,11,22]. Fujino et al. found that urgent PCI was less often performed for patients presenting without ischemic pain, door-to-balloon time was longer for STEMI patients presenting without ischemic pain, and that in-hospital mortality was higher in the group without ischemic pain (19.5 % vs 3.3 %) [11].

Within the literature, the debate regarding sex differences in MI symptom presentation continues primarily due to disagreeing conclusions drawn from study designs using different symptom definitions. A 2019 study by Ferry et al. [23] explored the impact of sex-specific diagnostic criteria in the Fourth Universal Definition of Myocardial Infarction [24], utilizing prospectively recorded symptoms in suspected acute coronary syndrome patients to address concerns of ascertainment bias and sex-specific troponin levels and excluding STEMI events [23]. Using the terminology "typical" and "atypical" pain symptoms, Ferry et al. defined "typical" pain as the presence of chest, arm, or jaw pain as well as nausea, vomiting,

sweating, dyspnea, and palpitations and "atypical" pain included epigastric or back pain, or any other non-"typical" pain [23]. The very terminology of "typical" and "atypical" suggests that "typical" pain is more common, and indeed it was, in both men and women. A 2018 study by Lichtman et al. found that among young patients with MI, 90 % of both men and women presented with chest pain, pressure, tightness, or discomfort [25]. DeVon et al. recommend retiring the terms "typical" and "atypical" pain as they imply a "correct presentation of symptoms" that distracts from the clinical importance of timely arrival to the hospital, timely testing, and timely treatment [26]. Additionally, "atypical" is problematic because it often describes symptoms that are both non-ischemic and non-cardiac [2]. The 2021 AHA/ACC Clinical Practice Guideline for the Evaluation and Diagnosis of Chest Pain recommends describing symptoms to suggest origin, using the terms "cardiac", "possible cardiac", "noncardiac" to reduce ambiguity [2].

4.1. Delays in seeking care and treatment

It is important for patients who think they are having a heart attack to seek care even in the absence of ischemic symptoms. Women are more likely to delay seeking care compared to men, and therefore, may be more susceptible to complications related to untreated prolonged ischemia [7,9,27]. With the current focus on reducing total ischemic time (time from symptom onset to reperfusion) [3,14,28], it is important to improve symptom identification/ recognition by both the individuals in the general population and by health care providers. In addition to delays in patients initially seeking medical care, there may be further delays in obtaining ECGs [29] and delivering appropriate guideline-directed treatments after presentation to the medical system (i.e., door-to-balloon time for STEMI), as found in previous ARIC analyses [30]. Specifically, McGinn et al. reported a larger proportion of Black adults and women with delays in symptom onset to hospital arrival of 4 h in the ARIC community surveillance study [30]. In our analysis, fewer patients presenting without ischemic pain arrived to the hospital within 2 h of symptom onset. Furthermore, higher proportion of NSTEMI patients presented without ischemic pain compared to STEMI patients. Previous research shows that once under medical care, patients with NSTEMI often experience delays in treatment [7] or receive less invasive treatment [10] - delays which may be extended even more when presenting without ischemic symptoms.

4.2. Strengths and limitations

A strength of our study is the use of physician ascertained event classification in addition to a standardized computer algorithm that considered ischemic pain, cardiac biomarkers, and ECG evidence uniformly across the 2005 to 2019 study period. The physician panel considers information from family interviews, hospital record abstractors, and clinic examiners in addition to the standardized computer algorithm information. Another strength of this analysis is that the ARIC study is based in 4 communities in multiple regions of the US. Limitations of these analyses include possible race-region confounding, inability to further subtype MI into Type 1 or Type 2 based on recent redefinitions of MI events, retrospective data analysis and pre-set data collection, and symptom recall issues that may introduce ascertainment bias. Only participants self-identifying as white or black were included. Regional variations in MI treatment may confound the relationship between MI without ischemic pain and mortality. Future studies that can separate race/ethnicity

from geographical location should explore the relationship between race/ethnicity and MI presenting without ischemic pain. Data was abstracted from medical charts retrospectively, and limited to information available in the medical chart and vital statistic records. For example, while time from symptom onset to hospital arrival or treatment was available, door-to-balloon time was not. It is of course possible that information on ischemic pain used in these analyses may be biased for various reasons such as practitioners recording of pain differently for different types of patients or patients may not accurately recall hour of symptom onset or may describe their pain differently.

4.3. Next steps

While there has been progress in the use of MI Pathway protocols and decreased door-to-balloon times (for STEMI) [28], registry data show persistent disparities with delayed treatment initiation in women, minorities, and other subgroups [9,27,31,32]. Given our findings that MI without ischemic pain carried a higher 28-day case fatality that could be explained by treatment patterns but not by race, sex or comorbidities, it is important to shift focus away from sex differences in symptom presentation so that timely intervention can be implemented [26]. A broader understanding of ischemic presentations that can occur without chest pain, regardless of sex, age, or comorbidities, is needed across the healthcare system [2]. Healthcare practitioners should utilize Clinical Decision Pathways and structured risk assessments for clinical decision making [2].

Public health education interventions intending to increase awareness of the various but serious possible symptoms of acute coronary syndromes (e.g., ischemic symptoms without chest pain) have been more effective at reducing prehospital delay than those educating patients about chest pain [33]. Efforts should continue to empower patients to take appropriate care seeking behaviors, including use of emergency medical transport, ideally developed and executed with the input of implementation scientists. In clinical practice, healthcare practitioners should be encouraged to use validated risk scores to triage possible acute coronary syndrome patients, as many of these risk scores utilize factors beyond chest pain, such as ECG changes and positive cardiac biomarker tests. Implementation of MI Pathway protocols may reduce disparities in in-hospital complications or case fatality as a function of treatment delay or under-treatment [3,34].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Funding

References

[1]. Mehta LS, et al. , Acute myocardial infarction in women : a scientific statement from the American Heart Association, Circulation 133 (2016).

[2]. Gulati M, et al. , 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of Chest pain: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines, Circulation 144 (2021) e368–e454.

[3]. Zègre-Hemsey JK, Burke LA, DeVon HA, Patient-reported symptoms improve prediction of acute coronary syndrome in the emergency department, Res. Nurs. Health 41 (2018) 459–468. [PubMed: 30168588]

[4]. DeVon HA, Rosenfeld A, Steffen AD, Daya M, Sensitivity, specificity, and sex differences in symptoms reported on the 13-item acute coronary syndrome checklist, J. Am. Heart Assoc. 3 (2014) 1–9.

[5]. Saczynski JS, et al. , Trends in prehospital delay in patients with acute myocardial infarction (from the Worcester Heart Attack Study), Am. J. Cardiol. 102 (2008) 1589–1594. [PubMed: 19064010]

[6]. O'Donnell S, McKee G, Mooney M, O'Brien F, Moser DK, Slow-onset and fast-onset symptom presentations in acute coronary syndrome (ACS): new perspectives on prehospital delay in patients with ACS, J. Emerg. Med. 46 (2014) 507–515. [PubMed: 24126070]

[7]. Moser DK, et al., in: Reducing Delay in Seeking Treatment by Patients With Acute Coronary Syndrome and Stroke A Scientific Statement From the American Heart Association Council on Cardiovascular Nursing and Stroke Council, 2006, pp. 168–182, 10.1161/CIRCULATIONAHA.106.176040.

[8]. Cannon AR, et al. , Use of prehospital 12-lead electrocardiography and treatment times among ST-elevation myocardial infarction patients with atypical symptoms, Acad. Emerg. Med. 21 (2014) 892–898. [PubMed: 25155289]

[9]. Bugiardini R, et al. , Delayed care and mortality among women and men with myocardial infarction, J. Am. Heart Assoc. 6 (2017) 1–10.

[10]. Canto AJ, Kiefe CI, Goldberg RJ, Rogers WJ, Differences in symptom presentation and hospital mortality according to type of acute myocardial infarction, Am. Heart J. 163 (2006) 572–579.

[11]. Fujino M, et al. , Impact of symptom presentation on in-hospital outcomes in patients with acute myocardial infarction, J. Cardiol. 70 (2016) 1–6.

[12]. Coventry LL, et al. , Characteristics and outcomes of MI patients with and without chest pain: a cohort study, Heart Lung Circ. 24 (2015) 796–805. [PubMed: 25797327]

[13]. Rousan TA, Pappy RM, Chen AY, Roe MT, Saucedo JF, Impact of diabetes mellitus on clinical characteristics, management, and in-hospital outcomes in patients with acute myocardial infarction (from the NCDR), Am. J. Cardiol. 114 (2014) 1136–1144. [PubMed: 25150136]

[14]. Doddipalli SR, Rajasekhar D, Vanajakshamma V, Sreedhar Naik K, Determinants of total ischemic time in primary percutaneous coronary interventions: a prospective analysis, Indian Heart J. 70 (2018) S275–S279. [PubMed: 30595273]

[15]. The ARIC Investigators, The atherosclerosis risk in communities (ARIC) study: design and objectives, Am. J. Epidemiol. 129 (1989) 689–702.

[16]. The ARIC Investigators, Manual 3: Surveillance Component Procedures Manual of Operations (version 6), 2015. https://www.cscc.unc.edu/aric/sites/default/files/public/manuals/Manual3_Ver%206.6_20151112_0.pdf.

[17]. Edlavitch SA, et al. , The effect of the number of electrocardiograms analyzed on cardiovascular disease surveillance: the Minnesota heart survey (MHS), J. Clin. Epidemiol. 43 (1990) 93–99. [PubMed: 2319286]

[18]. Edlavitch SA, Crow R, Burke GL, Baxter J, Secular trends in Q wave and non-Q wave acute myocardial infarction. The Minnesota Heart Survey, Circulation 83 (1991) 492–503. [PubMed: 1991368]

[19]. Rosamond WD, et al. , Twenty-two year trends in incidence of myocardial infarction, CHD mortality, and case-fatality in four US communities, 1987 to 2008, Circulation 1848–1857 (2012), 10.1161/CIRCULATIONAHA.111.047480. [PubMed: 22420957]

[20]. Amsterdam EA, et al. , 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association task force on practice guidelines, J. Am. Coll. Cardiol. 64 (2014) e139–e228. [PubMed: 25260718]

[21]. O'Gara PT, et al. , 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, Circulation 127 (2013) e362–e425. [PubMed: 23247304]

[22]. Dey S, et al. , Sex-related differences in the presentation, treatment and outcomes among patients with acute coronary syndromes: the global registry of acute coronary events, Heart 95 (2009) 20–26. [PubMed: 18463200]

[23]. Ferry AV, et al. , Presenting symptoms in men and women diagnosed with myocardial infarction using sex-specific criteria, J. Am. Heart Assoc. 8 (2019), e012307. [PubMed: 31431112]

[24]. Thygesen K, et al. , Fourth universal definition of myocardial infarction (2018), Circulation 138 (2018) e618–e651. [PubMed: 30571511]

[25]. Lichtman JH, et al. , Sex differences in the presentation and perception of symptoms among young patients with myocardial infarction: evidence from the VIRGO study (Variation in recovery: role of gender on outcomes of young AMI Patients), Circulation 137 (2018) 781–790. [PubMed: 29459463]

[26]. DeVon HA, Mirzaei S, Zègre-Hemsey J, Typical and atypical symptoms of acute coronary syndrome: time to retire the terms? J. Am. Heart Assoc. 9 (2020).

[27]. Mirzaei S, et al. , The association between symptom onset characteristics and prehospital delay in women and men with acute coronary syndrome, Eur. J. Cardiovasc. Nurs. 19 (2020) 142–154. [PubMed: 31510786]

[28]. Menees DS, et al. , Door-to-balloon time and mortality among patients undergoing primary PCI, Surv. Anesthesiol. 58 (2014) 162–163.

[29]. Zègre-Hemsey J, Sommargren CE, Drew BJ, Initial ECG acquisition within 10 minutes of arrival at the emergency Department in Persons with Chest Pain: time and gender differences, J. Emerg. Nurs. 37 (2011) 109–112. [PubMed: 21237383]

[30]. McGinn AP, et al. , Trends in prehospital delay time and use of emergency medical services for acute myocardial infarction: experience in 4 US communities from 1987–2000, Am. Heart J. 150 (2005) 392–400. [PubMed: 16169313]

[31]. Jneid H, et al. , Sex differences in medical care and early death after acute myocardial infarction, Circulation 118 (2008) 2803–2810. [PubMed: 19064680]

[32]. Udell JA, et al. , Sustained sex-based treatment differences in acute coronary syndrome care: insights from the American Heart Association get with the guidelines coronary artery disease registry, Clin. Cardiol. 41 (2018) 758–768. [PubMed: 29521450]

[33]. Hoschar S, Albarqouni L, Ladwig K-H, A systematic review of educational interventions aiming to reduce prehospital delay in patients with acute coronary syndrome, Open Heart 7 (2020), e001175. [PubMed: 32201586]

[34]. DeVon HA, Burke LA, Nelson H, Zerwic JJ, Riley B, Disparities in patients presenting to the emergency department with potentital acute coronary syndrome: it matters if you are black or white, Heart Lung 43 (2014) 270–277. [PubMed: 24992880]
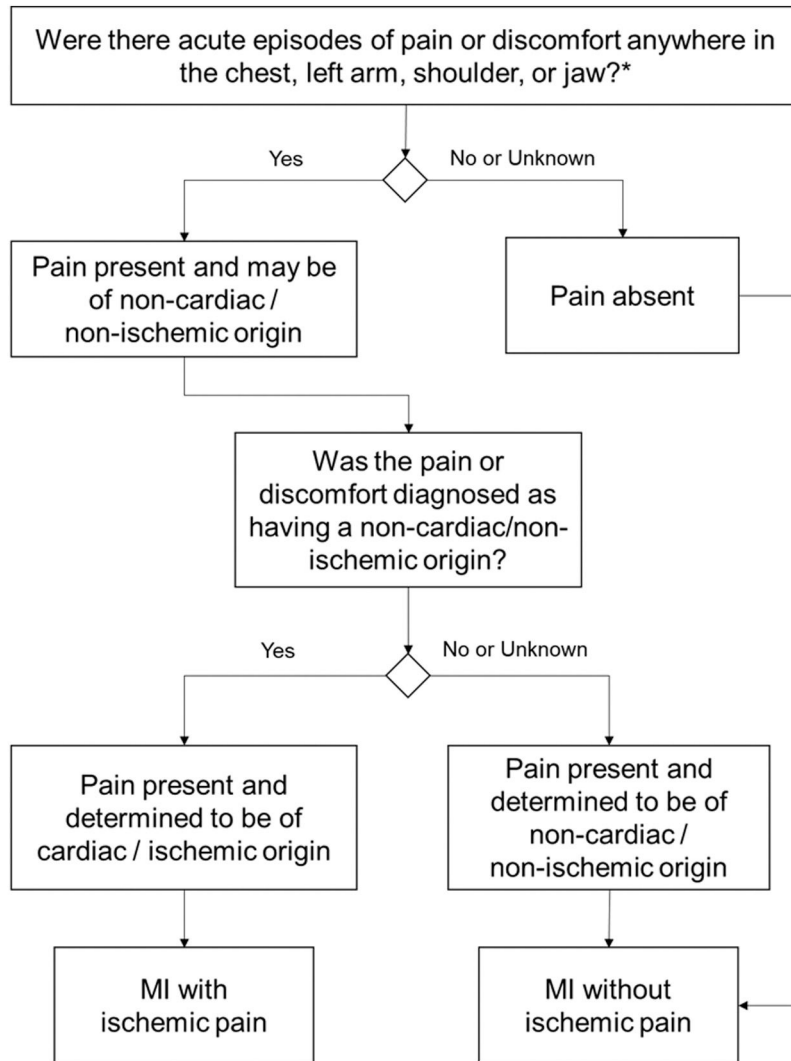
*For out-of-hospital events, pain within 72 hours prior to arrival at hospital. For in-hospital events, pain "in conjunction" with event.

Fig. 1.
Defining ischemic pain. The presence of pain is first determined by reviewing the medical record for acute episodes of pain or discomfort within 72 h of hospital arrival (out-of-hospital events) or in conjunction with in-hospital events. Pain is then classified as cardiac (ischemic) origin or non-ischemic origin by reviewing the full medical record. MI: myocardial infarction.

Fig. 2.
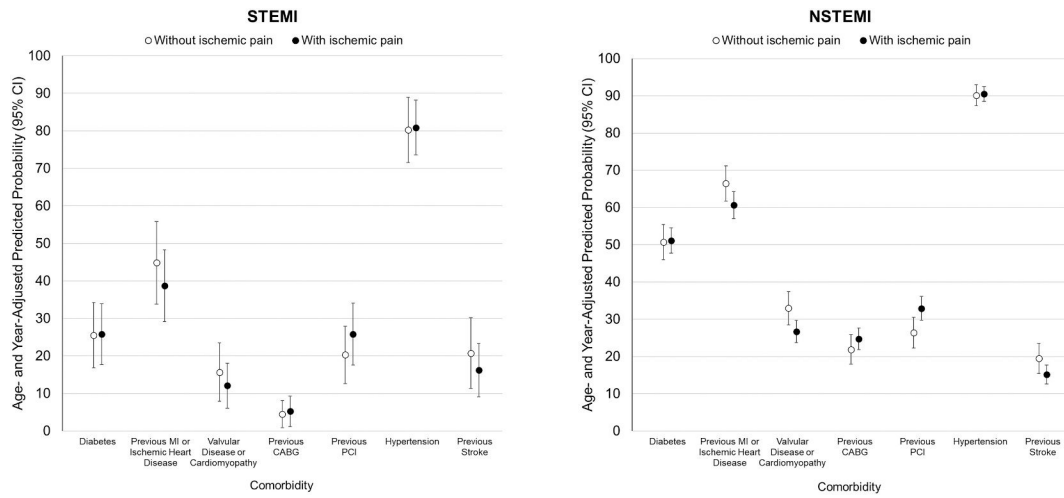Comorbidities among definite/probable MI events presenting with and without ischemic pain, ARIC cohort surveillance 2005–2019.

Predicted probabilities and 95 % confidence intervals were estimated from margins after logistic regression adjusted for age at event and year of event and presented for STEMI and NSTEMI. MI: Myocardial infarction. STEMI: ST-segment elevated MI. NSTEMI: non-ST-segment elevated MI.
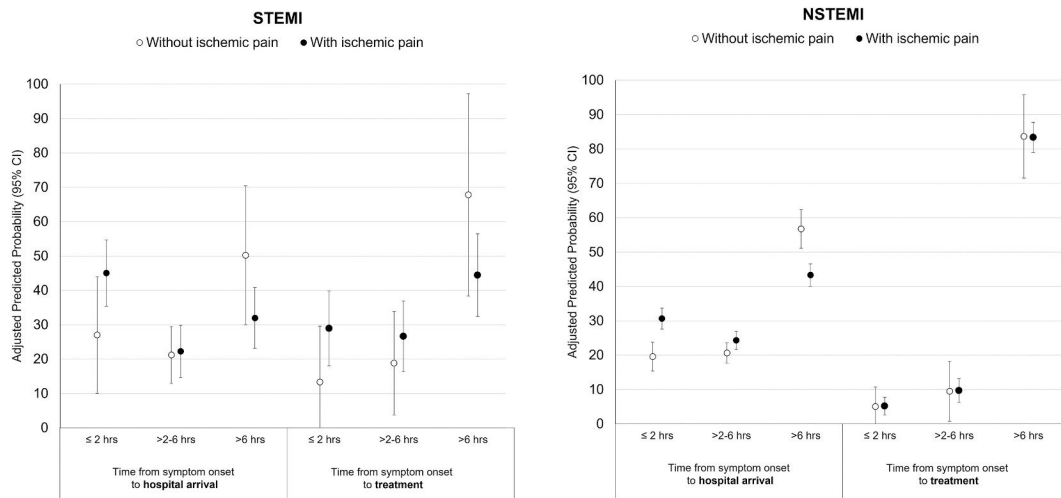
Fig. 3.

Time from symptom onset to hospital arrival and treatment among definite/probable hospitalized MI events presenting with and without ischemic pain, ARIC cohort surveillance 2005–2019.

Predicted probabilities and 95 % confidence intervals were estimated from margins after logistic regression adjusted for age at event and year of event and presented for STEMI and NSTEMI. Treatment included stent placement, intracoronary or intravenous reperfusion, coronary artery bypass graft, percutaneous coronary intervention/angioplasty, and atherectomy. MI: Myocardial infarction. STEMI: ST-segment elevated MI. NSTEMI: non-ST-segment elevated MI.

Fig. 4.

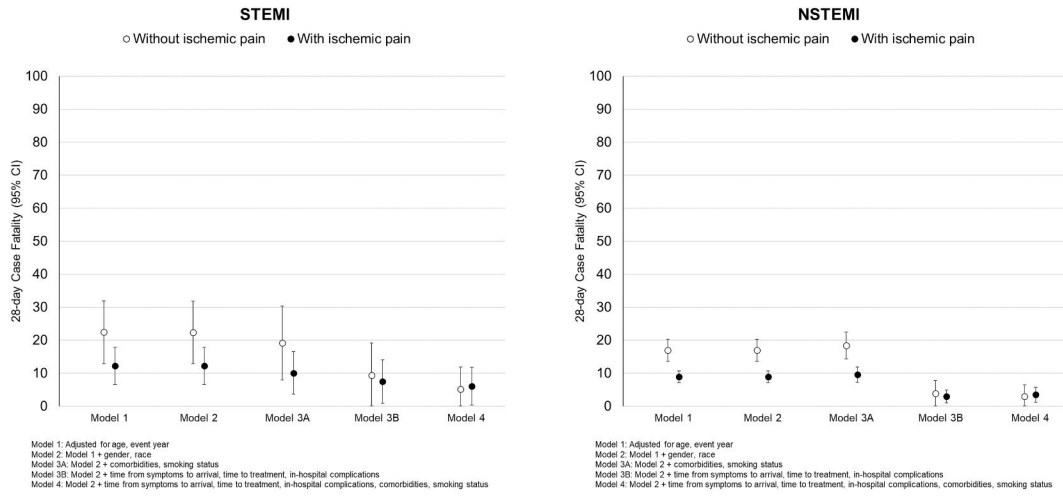Adjusted 28-day case fatality among definite/probable MI events presenting with and without ischemic pain, ARIC cohort surveillance 2005–2019.

Adjusted 28-day case fatality (predicted probabilities of dying from any cause within 28 days of MI event) and 95 % confidence intervals were estimated from margins after logistic regression and presented for STEMI and NSTEMI. Models were progressively adjusted from age and event year (Model 1) to include sex and race (Model 2), comorbidities and smoking status (Model 3A), time from symptom onset to arrival, time from symptom onset to treatment, and in-hospital complications (Model 3B) and all variables (Model 4). In-hospital complications included acute heart failure, pulmonary edema, pulmonary embolism, in-hospital stroke, pneumonia, cardiogenic shock, and ventricular fibrillation. MI: Myocardial infarction. STEMI: ST-segment elevated MI. NSTEMI: non-ST-segment elevated MI.

Table 1

Characteristics of patients with hospitalized MI events by MI subtype and ischemic pain presentation: ARIC cohort surveillance, 2005–2019.

	All MI			Unclassified MI			STEMI			NSTEMI		
	Total	Without ischemic pain	With ischemic pain	Total	Without ischemic pain	With ischemic pain	Total	Without ischemic pain	With ischemic pain	Total	Without ischemic pain	With ischemic pain
Hospitalized MI events	1711	546 (32 %)	1165 (68 %)	327 (19 %)	121 (37 %)	206 (63 %)	124 (7 %)	25 (20 %)	99 (80 %)	1260 (74 %)	400 (32 %)	860 (68 %)
Mean age (SD)	78.3 (6.7)	78.8 (6.6)	78.1 (6.7)	77.3 (6.9)	78.4 (7.0)	77.1 (6.9)	77.3 (6.9)	78.4 (7.0)	77.1 (6.9)	78.8 (6.6)	79.4 (6.5)	78.5 (6.6)
Age category												
<65 years	32 (1.9 %)	7 (1.3 %)	25 (2.2 %)	6 (1.8 %)	2 (1.7 %)	4 (1.9 %)	4 (3.2 %)	1 (4 %)	3 (3 %)	22 (1.8 %)	4 (1.0 %)	18 (2.1 %)
65–75 years	491 (29 %)	141 (26 %)	350 (30 %)	107 (33 %)	36 (30 %)	71 (35 %)	44 (36 %)	8 (32 %)	36 (36 %)	340 (27 %)	97 (24 %)	243 (28 %)
76–85 years	909 (53 %)	303 (55 %)	606 (52 %)	175 (54 %)	74 (61 %)	101 (49 %)	60 (48 %)	12 (48 %)	48 (48 %)	674 (54 %)	217 (54 %)	457 (53 %)
>85 years	279 (16 %)	95 (17 %)	184 (16 %)	39 (12 %)	9 (7.4 %)	30 (15 %)	16 (13 %)	4 (16 %)	12 (12 %)	224 (18 %)	82 (21 %)	142 (17 %)
Women	808 (47 %)	264 (48 %)	544 (47 %)	154 (47 %)	56 (46 %)	98 (48 %)	63 (51 %)	15 (60 %)	48 (48 %)	591 (47 %)	193 (48 %)	398 (46 %)
Black	452 (26 %)	151 (28 %)	301 (26 %)	67 (21 %)	24 (20 %)	43 (21 %)	28 (23 %)	10 (40 %)	18 (18 %)	357 (28 %)	117 (29 %)	240 (28 %)
Race-sex categories												
White males	702 (41 %)	216 (40 %)	486 (42 %)	147 (45 %)	57 (47 %)	90 (44 %)	47 (38 %)	6 (24 %)	41 (41 %)	508 (40 %)	153 (38 %)	355 (41 %)
White females	557 (33 %)	179 (33 %)	378 (33 %)	113 (35 %)	40 (33 %)	73 (35 %)	49 (40 %)	9 (36 %)	40 (40 %)	395 (31 %)	130 (33 %)	265 (31 %)
Black males	201 (12 %)	66 (12 %)	135 (12 %)	26 (8 %)	8 (7 %)	18 (9 %)	14 (11 %)	4 (16 %)	10 (10 %)	161 (13 %)	54 (14 %)	107 (12 %)
Black females	251 (15 %)	85 (16 %)	166 (14 %)	41 (13 %)	16 (13 %)	25 (12 %)	14 (11 %)	6 (24 %)	8 (8 %)	196 (16 %)	63 (16 %)	133 (16 %)
Teaching hospital[a]	561 (37 %)	164 (34 %)	397 (39 %)	75 (31 %)	25 (27 %)	50 (34 %)	37 (32 %)	6 (25 %)	31 (34 %)	449 (39 %)	133 (36 %)	316 (41 %)
Center, N (%)												
Forsyth Co., NC	465 (27 %)	151 (28 %)	314 (27 %)	67 (21 %)	23 (19 %)	44 (21 %)	41 (33 %)	5 (20 %)	36 (36 %)	357 (28 %)	123 (31 %)	234 (27 %)

	All MI			Unclassified MI			STEMI			NSTEMI		
	Total	Without ischemic pain	With ischemic pain	Total	Without ischemic pain	With ischemic pain	Total	Without ischemic pain	With ischemic pain	Total	Without ischemic pain	With ischemic pain
Jackson, MS	349 (20 %)	119 (22 %)	230 (20 %)	49 (15 %)	18 (15 %)	31 (15 %)	23 (19 %)	10 (40 %)	13 (13 %)	277 (22 %)	91 (23 %)	186 (22 %)
Minneapolis, MN	372 (22 %)	94 (17 %)	278 (24 %)	60 (13 %)	17 (14 %)	43 (21 %)	18 (15 %)	2 (8 %)	16 (16 %)	294 (23 %)	75 (19 %)	219 (26 %)
Washington Co., MD	525 (31 %)	182 (33 %)	343 (29 %)	151 (46 %)	63 (52 %)	88 (43 %)	42 (34 %)	8 (32 %)	34 (34 %)	332 (26 %)	111 (28 %)	221 (26 %)

Hospitalized MI events include all definite and probable MI events. Ischemic pain refers to cardiac pain. "Without ischemic pain" refers to definite or probable MI presenting without any pain, or with pain determined to be of noncardiac origin. MI: myocardial infarction; STEMI: ST-segment elevation MI, NSTEMI: non-ST-segment elevation MI.

[a] N = 212 missing information on teaching hospital classification.