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Original Contributions

COMPARISON OF THE ST-ELEVATION MYOCARDIAL INFARCTION (STEMI) VS. NSTEMI AND OCCLUSION MI (OMI) VS. NOMI PARADIGMS OF ACUTE MI

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☐ **Abstract Background: The current ST-elevation myocardial infarction (STEMI) vs. non-STEMI (NSTEMI) paradigm prevents some NSTEMI patients with acute coronary occlusion from receiving emergent reperfusion, in spite of their known increased mortality compared with NSTEMI without occlusion. We have proposed a new paradigm known as occlusion MI vs. nonocclusion MI (OMI vs. NOMI). Objective: We aimed to compare the two paradigms within a single population. We hypothesized that STEMI( ) OMI would have characteristics similar to STEMI(+) OMI but longer time to catheterization. Methods: We performed a retrospective review of a prospectively collected acute coronary syndrome population. OMI was defined as an acute culprit and either TIMI 0 2 flow or TIMI 3 flow plus peak troponin T > 1.0 ng/mL. We collected electrocardiograms, demographic characteristics, laboratory results, angiographic data, and outcomes. Results: Among 467 patients, there were 108 OMIs, with only 60% (67 of 108) meeting STEMI criteria. Median peak troponin T for the STEMI(+) OMI, STEMI( ) OMI, and no occlusion groups were 3.78 (interquartile range [IQR] 2.18 7.63), 1.87 (IQR 1.12 5.48), and 0.00 (IQR 0.00 0.08). Median time from arrival to catheterization was 41 min (IQR 23 86 min) for STEMI(+) OMI compared with 437 min (IQR 85 1590 min) for STEMI( ) OMI ($p < 0.001$). STEMI(+) OMI was more likely than STEMI( ) OMI to undergo catheterization within 90 min (76% vs. 28%; $p < 0.001$). Conclusions: STEMI( ) OMI patients had significant delays to catheterization but adverse outcomes more similar to STEMI(+) OMI than those with no occlusion. These data support the OMI/NOMI paradigm and the importance of further research into emergent reperfusion for STEMI( ) OMI.**

☐ **Keywords acute coronary syndrome; ST-segment elevation myocardial infarction; occlusion myocardial infarction; electrocardiogram; acute myocardial infarction**

INTRODUCTION

In patients with acute coronary syndrome (ACS), thrombolytic therapy and percutaneous coronary intervention (PCI) are intended to achieve reperfusion of acute coronary occlusion or near occlusion to salvage downstream myocardium, which is otherwise at imminent risk of irreversible infarction. The current guideline-recommended strategy for identifying patients with acute occlusion myocardial infarction (OMI) who will benefit from emergent reperfusion therapy is the ST-elevation myocardial

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infarction (STEMI) vs. non-STEMI (NSTEMI) paradigm. Because NSTEMI may be OMI or nonocclusion MI (NOMI), the STEMI/NSTEMI paradigm results in classification of many OMI as NSTEMI, and these patients do not receive rapid reperfusion (1). Approximately 25% to 30% of NSTEMI patients have acute total occlusion (OMI) discovered only on delayed cardiac catheterization, and they have an increased incidence of major adverse events compared with NSTEMI patients without OMI (nonocclusion MI [NOMI]), including in-hospital, short-term, and long-term mortality that are approximately twice as high (1). Conversely, 15% to 35% of STEMI activations are found to be false positives without a culprit lesion (2 4).

The STEMI vs. NSTEMI paradigm is based on the randomized controlled thrombolytic trials in the 1980s and 1990s in which the outcome measure was mortality, not angiographic coronary occlusion (5). Enrollment criteria were poorly defined, and analysis correlating electrocardiogram (ECG) findings with outcome benefit of thrombolytic therapy was limited to unmeasured and undefined ECG subgroups of ST elevation (STE), ST depression (STD), and "normal" (simply meaning neither STE nor STD in these studies) (5). Subsequent studies have found many ECG predictors of acute coronary occlusion other than STE (6). Nevertheless, many OMI have no specific ECG findings and must be diagnosed on the basis of high suspicion and ongoing symptoms with or without troponin and echocardiography, with confirmation by angiography (7 9). American and European NSTEMI guidelines recommend immediate angiography for suspected ACS with hemodynamic or electrical instability, or persistent symptoms, and the European guidelines recommend such evaluation when there is high suspicion, even in the absence of ECG or biomarker evidence of AMI (10,11). The STEMI/NSTEMI paradigm is dependent on STE and on STE meeting defined millimeter criteria; however, many OMI do not meet these criteria, have no STE at all, have other ECG features, or have a completely nondiagnostic ECG. We have proposed a different paradigm: the OMI/NOMI paradigm, which acknowledges the shortcomings of the STEMI/NSTEMI paradigm and includes more than just STE for making the emergent diagnosis of acute coronary occlusion (12,13). OMI is defined conceptually as acute coronary occlusion or near occlusion with insufficient collateral circulation, such that downstream myocardium will undergo imminent necrosis without reperfusion. Table 1 lists definitions and terminology of each paradigm, and Figures 1 and 2 visually show the ACS paradigm before and after the incorporation of the OMI vs. NOMI concept. OMI has been used as the outcome definition for many studies of ECG interpretation over the past 10 to 15 years (14 25). To date, there has been no study directly exploring the relationship and differences between the two paradigms.

Goals of This Investigation

We aimed to explore the differences between these two classification systems within a single ACS patient population. Specifically, we aimed to compare the differences between STEMI(+) OMI and STEMI( ) OMI. We hypothesized that STEMI( ) OMI is a substantial subgroup with similar characteristics to the STEMI(+) OMI group, with the exception of the time from presentation to cardiac catheterization.

MATERIALS AND METHODS

Study Design and Setting

This investigation was a planned substudy of the Diagnosis of Occlusion MI and Reperfusion by Interpretation of the Electrocardiogram in Acute Thrombotic Occlusion (DOMI ARIGATO) database (ClinicalTrials.gov ID:

Table 1. Definitions and Terminology Among Paradigms

Definitions and Terminology of Paradigms	
STEMI	Refers to AMI with ECG findings meeting the definition of STEMI criteria in the fourth universal definition of MI (6)
False-positive STEMI	Refers to a patient with ECG features meeting formal STEMI criteria, but the ST elevation is not a result of ischemia, and there is both no culprit lesion and no AMI.
True-positive STEMI STEMI(+) OMI	Refers to a patient with ECG features meeting formal STEMI criteria, who is found to have OMI as the cause of the STE and the AMI.
Occlusion MI (OMI)	Refers to type 1 acute coronary syndrome involving acute occlusion or near occlusion of a major epicardial coronary vessel with insufficient collateral circulation, resulting in imminent necrosis of downstream myocardium without emergent reperfusion. OMI is the anatomic and pathophysiologic substrate of STEMI, but not all OMI manifests as STEMI.
Nonocclusion MI (NOMI) NSTEMI without occlusion	Refers to AMI without angiographic, laboratory, or clinical evidence of OMI.
STEMI(–) OMI NSTEMI with occlusion	Refers to OMI without the ECG meeting STEMI criteria.

AMI acute myocardial infarction; ECG electrocardiogram; STEMI ST-segment elevation myocardial infarction.

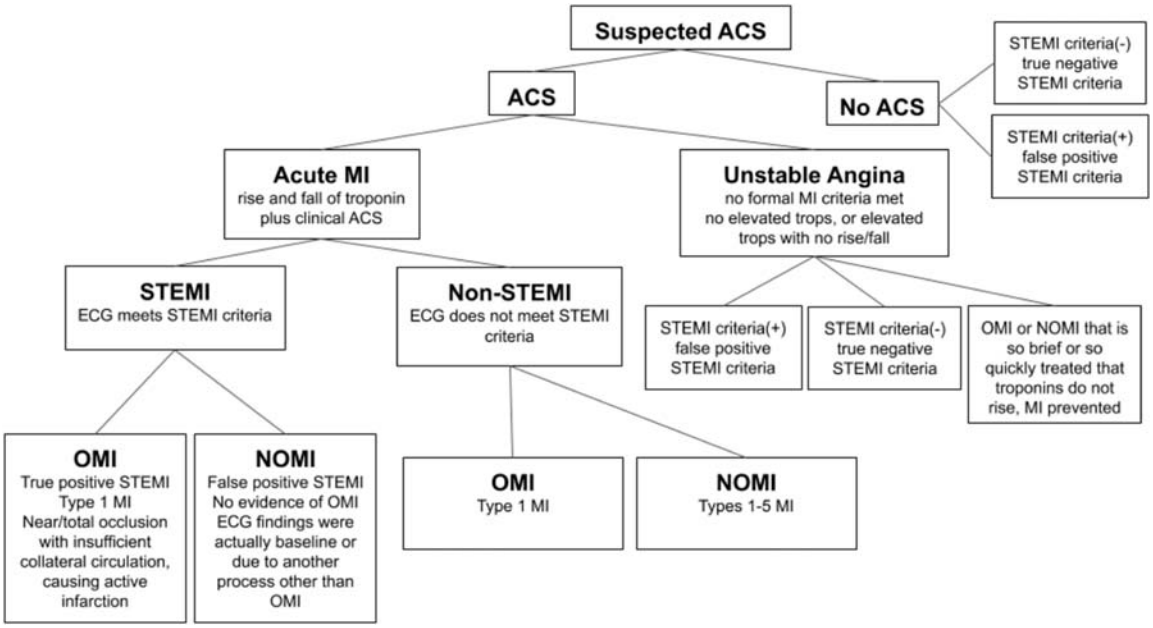

Figure 1. The acute coronary syndrome (ACS) spectrum using the ST-segment elevation myocardial infarction (STEMI) vs. non-STEMI paradigm primarily. The current paradigm of MI divides acute MI into STEMI and non-STEMI based on the electrocardiogram (ECG). Occlusion myocardial infarction (OMI) and nonocclusion myocardial infarction (NOMI) are possible in both STEMI and non-STEMI categories.

NCT03863327), which is a two-site collaboration designed to investigate electrocardiographic features of OMI. We reviewed a prospectively collected cohort of consecutive patients who presented to the emergency department (ED) with symptoms concerning for possible ACS at a suburban, academic hospital ED or the surrounding community EDs for which the academic center serves as a cardiac catheterization referral center. Stony Brook University Hospital has 695 beds, and the ED sees more than 100,000 patients per year, with

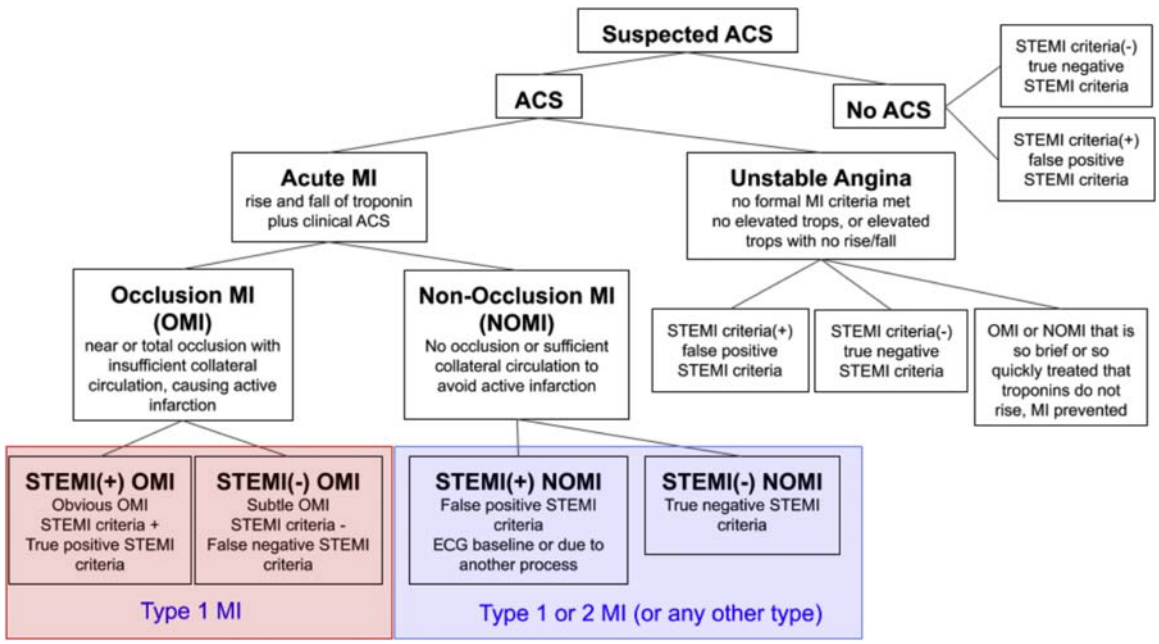

Figure 2. Central illustration: The acute coronary syndrome (ACS) spectrum using the occlusion myocardial infarction (OMI) vs. nonocclusion myocardial infarction (NOMI) paradigm primarily. The proposed paradigm of MI divides acute MI into OMI and NOMI. OMI are those for whom thrombolytics and percutaneous coronary intervention were conceptually designed and indicated, but many OMI do not manifest ST-segment elevation myocardial infarction (STEMI) criteria. ECG = electrocardiogram.

Table 2. Clinical Characteristics of all Patients in Each Subgroup of Myocardial Infarction Classification

Character st c	A Pat ents (n = 467)	A OM (n = 108)	STEM (+) OM (n = 67)	STEM (–) OM (n = 41)	A NSTEM (n = 167)	A NOM (n = 126)	A AM (n = 234)	No Occ us on (n = 359)
Age, y, mean (SD)	64.92 (12.84)	63.77 (12.47)	62.04 (13.31)	66.59 (10.51)	66.68 (13.07)	66.71 (13.83)	65.35 (13.28)	65.27 (12.94)
Fema e, n (%)	171 (36.6)	30 (27.8)	19 (28.4)	11 (26.8)	66 (39.5)	55 (43.7)	85 (36.3)	141 (39.3)
Caucas an, n (%)	396 (84.8)	91 (84.3)	54 (80.6)	37 (90.2)	144 (86.2)	107 (84.9)	198 (84.6)	305 (85.0)
H span c or Lat no, n (%)	31 (6.6)	8 (7.4)	8 (11.9)	0 (0.0)	9 (5.4)	9 (7.1)	17 (7.3)	23 (6.4)
Known CAD, n (%)	212 (45.4)	22 (20.4)	10 (14.9)	12 (29.3)	78 (46.7)	66 (52.4)	88 (37.6)	190 (52.9)
Pr or CABG, n (%)	60 (12.8)	8 (7.4)	3 (4.5)	5 (12.2)	29 (17.4)	24 (19.0)	32 (13.7)	52 (14.5)
Pr or CVA, n (%)	33 (7.1)	8 (7.4)	2 (3.0)	6 (14.6)	14 (8.4)	8 (6.3)	16 (6.8)	25 (7.0)
CKD, n (%)	47 (10.1)	8 (7.4)	3 (4.5)	5 (12.2)	24 (14.4)	19 (15.1)	27 (11.5)	39 (10.9)
CHF, n (%)	59 (12.6)	4 (3.7)	2 (3.0)	2 (4.9)	26 (15.6)	24 (19.0)	28 (12.0)	55 (15.3)
D abetes, type 2, n (%)	162 (34.7)	31 (28.7)	20 (29.9)	11 (26.8)	61 (36.5)	50 (39.7)	81 (34.6)	131 (36.5)
HLD, n (%)	286 (61.2)	57 (52.8)	32 (47.8)	25 (61.0)	106 (63.5)	81 (64.3)	138 (59.0)	229 (63.8)
HTN, n (%)	339 (72.6)	72 (66.7)	45 (67.2)	27 (65.9)	120 (71.9)	93 (73.8)	165 (70.5)	267 (74.4)
Obes ty (BM > 30), n (%)	230 (49.3)	45 (41.7)	33 (49.3)	12 (29.3)	79 (47.3)	67 (53.2)	112 (47.9)	185 (51.5)
PVD, n (%)	19 (4.1)	2 (1.9)	0 (0.0)	2 (4.9)	10 (6.0)	8 (6.3)	10 (4.3)	17 (4.7)
Smok ng h story, n (%)	271 (58)	68 (63.0)	42 (62.7)	26 (63.4)	106 (63.5)	80 (63.5)	148 (63.2)	203 (56.5)
Fam y h story of CAD, n (%)	191 (40.9)	56 (51.9)	38 (56.7)	18 (43.9)	64 (38.3)	46 (36.5)	102 (43.6)	135 (37.6)
Transfer, n (%)	110 (23.6)	25 (23.1)	16 (23.9)	9 (22.0)	42 (25.1)	33 (26.2)	58 (24.8)	85 (23.7)

AM = acute myocard a nfarct on; BM = body mass ndex; CABG = coronary artery bypass graft ng; CAD = coronary artery d sease; CHF = congest ve heart fa ure; CKD = chron c k dney d sease; CVA, cerebrovascu ar acc dent; HLD = hyper p dem a; HTN = hypertens on; NOM = nonocc us on M ; NSTEM = non-ST-segment e evat on M ; OM = occ us on M ; PVD = per phera vascu ar d sease; SD = standard dev at on; STEM = ST-segment e evat on myocard a nfarct on.

approximately 125 catheterization laboratory activations per year. We did not use patients from the other clinical site in this substudy because they were not prospectively collected consecutive patients. Because of the retrospective design, we received Institutional Review Board approval with waiver of informed consent and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in *a priori* approval by the institution's human research committee.

Selection of Participants

Participants were prospectively collected on admission from the ED to the cardiology service by means of two continuous databases. Database 1 prospectively collects all consecutive patients admitted to cardiology with possible ACS and scheduled for urgent or emergent cardiac catheterization. Database 2 prospectively collects all consecutive patients for whom the cardiology interventionalist is called for ED consultation of possible emergent PCI (usually because of STEMI criteria on ECG, ongoing ACS with ischemia not resolving with medical therapy, or other indications for immediate angiography). We combined both databases during a 6-month time period in 2017 and excluded duplicate presentations. From the resulting combined list of unique patient encounters we excluded patients without an ECG in our electronic medical record.

Data Collection and Measurements

Charts were reviewed by four emergency medicine (EM) resident physicians. Data abstractors were trained using a standardized data coding manual. The primary and senior authors (H.P.M. and S.W.S.) were available for on-demand questions, feedback, and re-training. All data including demographic characteristics, clinical and laboratory features, ECGs, and angiographic results were collected and managed using the standardized, web-based Research Electronic Data Capture (REDCap) site hosted by an academic tertiary hospital (26). We collected all available transfer, prehospital, and study site ECGs. For each patient, one investigator (H.P.M.), blinded to all clinical and outcome data, reviewed all available transfer, prehospital, and the first precatheterization study site ECGs for the presence of formal STEMI criteria. STEMI criteria were defined and measured (from the QRS onset [PQ junction] to the J-point in millimeters) according to the fourth universal definition of MI (27). If any of the ECGs met STEMI criteria, the patient was considered to have an STEMI(+) ECG. Otherwise, the patient was considered to have an STEMI( ) ECG. Interobserver variation to the nearest 0.5 mm has been previously established within our author group (21,23,28,29). For

further assurance of interrater reliability, all cases meeting OMI criteria were reviewed for the presence of STEMI criteria by a cardiology fellow blinded to the outcome and the study goals.

Although the diagnosis of OMI vs. NOMI was adjudicated by the research team, the diagnosis of any AMI among patients who did not undergo angiography was collected from the final diagnosis on the chart rather than adjudicated separately. The retrospective diagnosis of OMI was reproduced from prior studies, composed of either "confirmed OMI" on cardiac catheterization (defined as an acute culprit lesion with TIMI 0 2 flow) or "presumed OMI with significant cardiac outcome," defined as any of the following: angiogram showing an acute but nonocclusive culprit lesion with highly elevated biomarkers (contemporary troponin T $\geq$ 1.0 ng/mL; Roche Diagnostics Elecsys, Indianapolis, IN [reference range $\leq$ 0.01 ng/mL); if no angiography was performed, then highly elevated biomarkers and a new or assumed new regional wall motion abnormality on echocardiography; or ECG positive for STEMI with death before attempted emergent catheterization (20 22). Formal adjudication was made with all available data, including ECGs, troponins, and angiogram results. The definition of "highly elevated" cardiac biomarkers was chosen previously as the most accurate cutoff for differentiating STEMI from NSTEMIs using various biomarker assays, and has subsequently been internally and externally validated (7,21,22,30 33).

Outcomes

The primary objective was to compare infarct size in the STEMI(+) OMI vs. the STEMI( ) OMI group, as well as time from presentation to cardiac catheterization between the STEMI(+) OMI and STEMI( ) OMI groups. Infarct size was estimated by peak troponin (33 36). Secondarily, we performed exploratory analyses on the presence of wall motion abnormalities, medication administration, and adverse outcomes between groups.

Analysis

Subject characteristics and outcomes were compared between groups using Mann-Whitney U or Kruskal-Wallis tests for continuous measurements and Pearson χ^2 or Fisher exact tests for categorical measures. All tests were two-sided, and statistical significance was accepted at the 0.05 level. Descriptive statistics, statistical tests, and graphs were performed with Microsoft Excel, version 1905 (Redmond, WA).

RESULTS

Subject Identification

Figure 3 shows the results of our inclusion and exclusion process, resulting in the final study population of 467 unique patient encounters.

Characteristics of Study Subjects

Overall population. Table 2 shows the clinical characteristics of all patients in each group and Table 3 shows the clinical outcomes. AMI was present in 234 patients (50.1%). OMI criteria was met in 108 cases (23.1%). Blinded reviewer 1 categorized 67 of 108 OMIs as STEMI, and blinded reviewer 2 categorized 59 as STEMI. There was agreement in 87% of cases, with κ

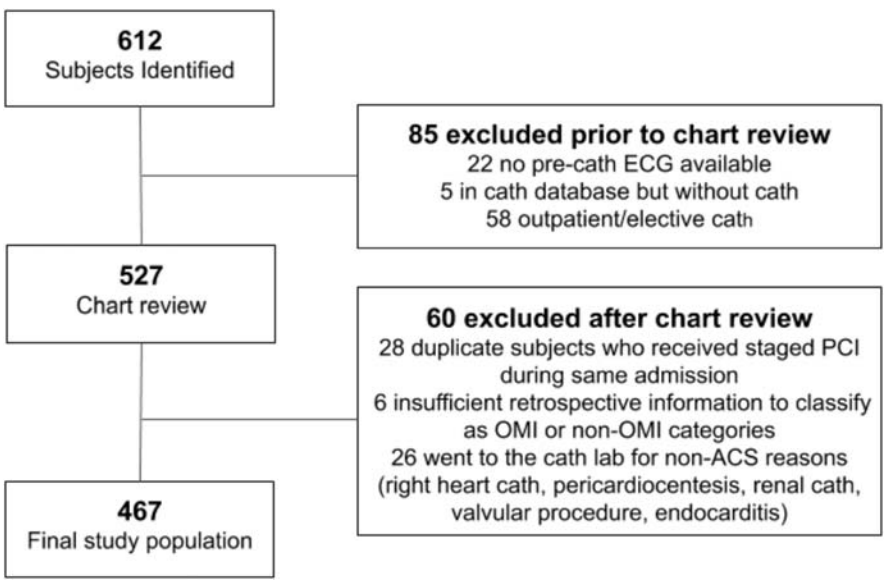

Figure 3. Flow chart showing initial subjects identified, exclusions, and final study population. ACS = acute coronary syndrome; ECG = electrocardiogram; OMI = Occlusion myocardial infarction; PCI = percutaneous coronary intervention.

Table 3. Clinical Outcomes of all Patients and Each Subgroup of Myocardial Infarction Classification

Outcomes	A Pat ents (n = 467)	A OM (n = 108)	STEM (+) OM (n = 67)	STEM (–) OM (n = 41)	A NSTEM (n = 167)	A NOM (n = 126)	A AM (n = 234)	No Occ us on (n = 359)
Presented n card ac arrest, n (%)	7 (2.0)	4 (5.1)	3 (6.1)	1 (3.3)	3 (2.6)	2 (2.3)	6 (3.6)	3 (1.1)
Card ac arrest dur ng or mmed ate y pr or to v s t, n (%)	22 (4.7)	11 (10.2)	7 (10.4)	4 (9.8)	13 (7.8)	9 (7.1)	20 (8.5)	11 (3.1)
Emergent Act vat on by ED, n (%)	105 (22.5)	81 (75.0)	62 (92.5)	19 (46.3)	35 (21.0)	16 (12.7)	97 (41.5)	24 (6.7)
Length of stay, d, mean (SD)	4.9 (7.1)	6.0 (9.1)	5.9 (9.0)	6.1 (9.5)	6.2 (8.2)	6.2 (7.7	6.1 (8.4)	4.6 (6.3)
Length of stay, d, med an (QR)	2.5 (1.4–6.1)	3.3 (1.7–5.9)	3.4 (1.9–6.4)	3.1 (1.5–5.2)	3.4 (1.5–7.5)	3.8 (1.5–8.2)	3.4 (1.6–7.3)	2.4 (1.2–6.2)
AM , n (%)	234 (50.3)	108 (100.0)	67 (100.0)	41 (100.0)	167 (100.0)	126 (100.0)	234 (100.0)	126 (35.3)
n-hosp ta morta ty, n (%)	13 (2.8)	5 (4.6)	4 (6.0)	1 (2.4)	8 (4.8)	7 (5.6)	12 (5.1)	8 (2.2)
D scharge to hosp ce, n (%)	2 (0.5)	2 (2.4)	1 (1.9)	1 (3.1)	1 (0.8)	0 (0.0)	2 (1.1)	0 (0.0)
3-m post-hosp ta morta ty, n (%)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)	2 (1.7)	2 (0.9)	2 (0.6)
F rst tropon n negat ve, n (%)	238/461 (51.6)	28/108 (25.9)	17/67 (25.4)	11/41 (26.8)	39/164 (23.8)	28/123 (22.8)	56/231 (21.5)	210/353 (59.5)
n t a tropon n, ng/mL, mean (SD)	0.27 (0.95)	0.95 (1.79	1.01 (1.99)	0.84 (1.40)	0.34 (0.79)	0.17 (0.29)	0.53 (1.30)	0.07 (0.19)
n t a tropon n, ng/mL med an (QR)	0 (0–0.11)	0.22 (0–1.05)	0.22 (0.01–1.01)	0.12 (0–1.27)	0.06 (0.01–0.28)	0.06 (0.01–0.20)	0.08 (0.01–0.35)	0 (0–0.04)
Peak tropon n, ng/mL, mean (SD); n	1.31 (3.34); 425	5.14 (5.25); 101	5.50 (4.48); 66	4.44 (6.47); 35	1.34 (3.65); 143	0.33 (0.43); 108	2.65 (4.37); 209	0.12 (0.29); 324
Peak tropon n, ng/mL, med an (QR)	0.03 (0.00–0.78)	3.51 (1.46–7.56)	3.78 (2.18–7.63)	1.87 (1.12–5.48)	0.31 (0.09–0.96)	0.19 (0.05–0.40)	0.81 (0.16–3.29)	0.00 (0.00–0.08)
Pr or ECG ava ab e, n (%)	287 (61.5)	46 (42.6)	23 (34.3)	23 (56.1)	99 (59.3)	76 (60.3)	122 (52.1)	241 (67.1)
TTE performed, n (%)	335 (71.7)	105 (97.2)	65 (97.0)	40 (97.6)	138 (82.6)	98 (77.8)	203 (86.8)	230 (64.1)
Ang ography performed, n (%)	448 (95.9)	107 (99.1)	67 (100.0)	40 (97.6)	163 (97.6)	123 (97.6)	230 (98.3)	341 (95.0)
T me from arr va at n t a ED to catheter zat on, m n, mean (SD)	2346 (3063)	861 (2949)	425 (2466)	1591 (3531)	2758 (3421)	3137 (3311)	2078 (3341)	2812 (2952)
T me from arr va at n t a ED to catheter zat on, m n, med an (QR)	1361 (265–3094)	71 (30–367)	41 (23–86)	437 (85–1590)	1510 (538–3454)	1830 (1165–4244)	962 (62–2569)	1710 (1044–4071)
Catheter zat on w th n 90 m n, n/N (%)	82/448 (18.3)	62/107 (58.0)	51/67 (76)	11/40 (28)	20/163 (12.3)	9/123 (7.3)	71/230 (30.9)	20/341 (5.9)

AM = acute myocard a nfarct on; ECG = e ectrocard ogram; ED = emergency department; QR = nterquart e range; NOM = nonocc us on M ; NSTEM = non-ST-segment e evat on M ; OM = occ us on M ; SD = standard dev at on; STEM = ST-segment e evat on myocard a nfarct on; TTE = transthorac c echocard ogram.

value 0.735 (95% confidence interval 0.607 0.863). Final analysis was performed with the more conservative 67 STEMI classifications, resulting in 67 STEMI(+) OMIs (62% of all OMI) and 41 STEMI( ) OMIs (38% of all OMI). By the STEMI vs. NSTEMI paradigm there were 67 STEMIs and 167 NSTEMIs, and by the OMI vs. NOMI paradigm there were 108 OMIs and 126 NOMIs. The catheterization laboratory was emergently activated by the ED in 105 patients (22.5%, 62 STEMI[+] OMI, 19 STEMI[ ] OMI, and 24 no occlusion) and subsequently cancelled in 7 cases. Coronary angiography was performed in 448 cases (96%), with 82 patients (18.3%) receiving catheterization in < 90 min of arrival. Twenty-two patients (4.7%) had prehospital or ED cardiac arrest with return of spontaneous circulation, 7 of whom arrived to the ED in cardiac arrest. Ventricular fibrillation was the initial cardiac arrest rhythm in 77% of all cardiac arrests.

Outcomes

Comparison of STEMI(+) OMI, STEMI( ) OMI, and no occlusion groups. Peak troponin T Mean (standard deviation [SD]) peak cardiac troponin T for the STEMI(+) OMI, STEMI( ) OMI, and no occlusion groups were 5.36 (4.43) ng/mL, 4.44 (6.47) ng/mL, and 0.12 (0.29) ng/mL ($p < 0.001$ for both STEMI[+] and STEMI[ ] compared with the no occlusion group; $p = 0.021$ between STEMI[+] and STEMI[ ] OMI, above the acceptable cutoff using the Bonferroni corrected α value of 0.05/3 = 0.017). Median peak troponin T were 3.78 (interquartile range [IQR] 2.18 7.63), 1.87 (IQR 1.12 5.48), and 0.00 (IQR 0.00 0.08), respectively. The difference between the medians in STEMI(+) and STEMI( ) OMI groups was not statistically significant ($p = 0.026$ by Kruskal-Wallis, with Bonferroni correction). Median peak troponins of both STEMI(+) and STEMI( ) were statistically greater than the no occlusion group, each with $p < 0.0001$. Figure 4 shows the peak troponin levels among the groups of the STEMI vs. NSTEMI paradigm, and Figure 5 shows the same information with the NSTEMI group additionally subdivided into STEMI( ) OMI (NSTEMI with occlusion) and NOMI (NSTEMI without occlusion).Angiographic Outcomes

Of the 108 OMIs by TIMI 0 2 criteria, 55 of 67 (82%) STEMI(+) OMI patients and 29 of 41 (71%) STEMI( ) OMI patients had TIMI 0 2 flow at the time of

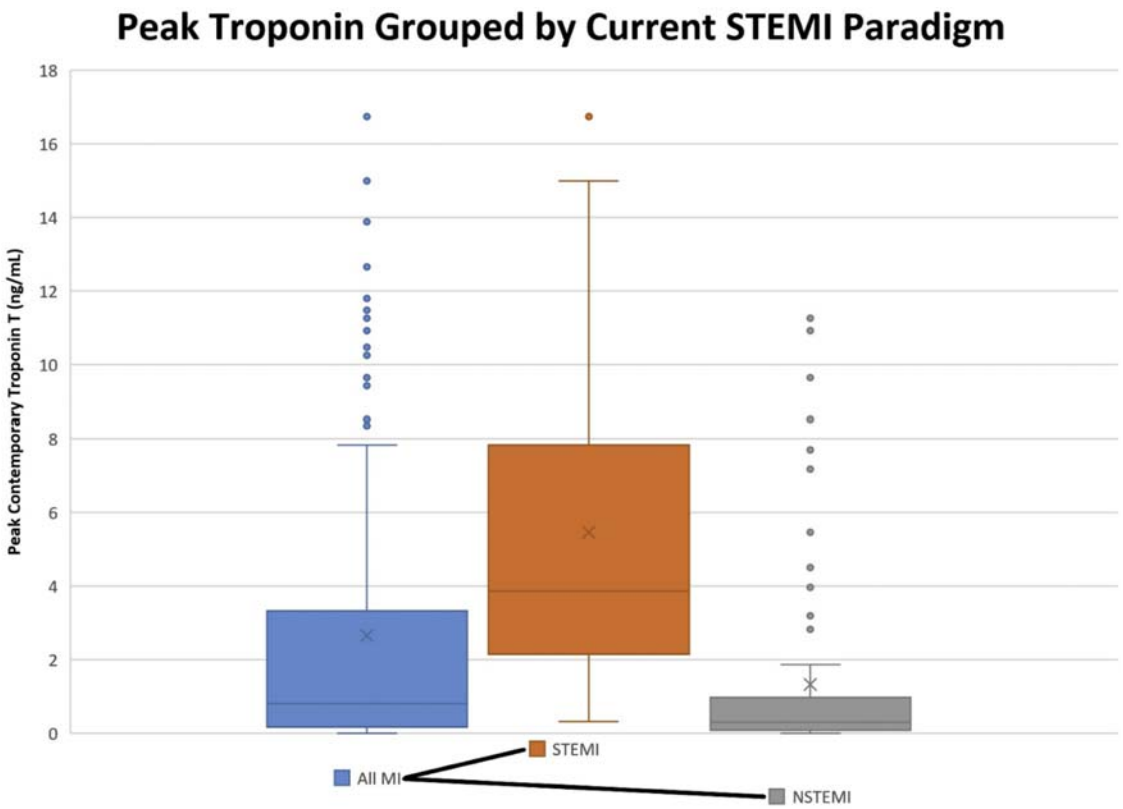

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Figure 4. Box and whisker plots showing the distributions of peak cardiac troponin T among the categories of the current acute myocardial infarction (MI) paradigm. The current paradigm appears to show effective dichotomization into categories for which our guidelines recommend for ST-segment elevation myocardial infarction (STEMI) and against non-STEMI (NSTEMI) emergent reperfusion. However, comparison with Figure 5 reveals the missed occlusion myocardial infarctions in the NSTEMI group.

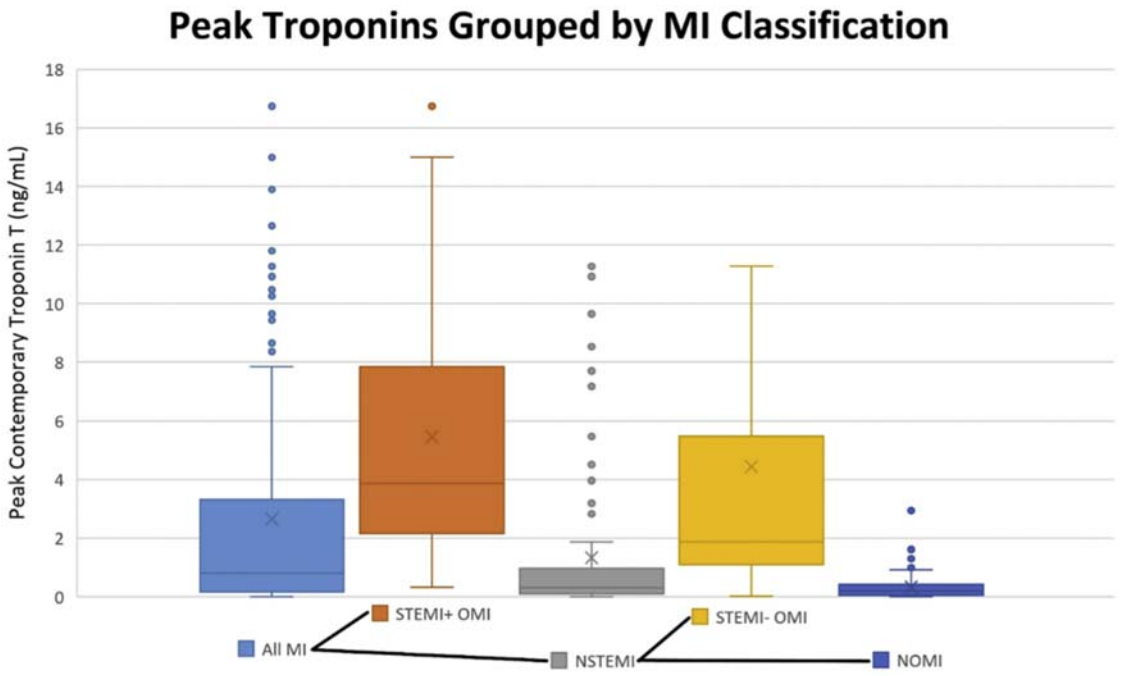

Figure 5. Box and whisker plots showing the distributions of peak cardiac troponin T among the categories of acute myocardial infarction (MI). This shows the information in Figure 4, but with the non-ST-segment elevation myocardial infarction (NSTEMI) group additionally broken down into its component subgroups: STEMI(–) OMI (NSTEMI with occlusion) and NOMI (NSTEMI without occlusion). This reveals a subset of patients in the NSTEMI group, which have the same angiographic disease as STEMI(+) occlusion MI but do not typically receive emergent catheterization due our current STEMI paradigm.

catheterization (p = 0.2172). Twelve (18%) STEMI(+) OMI and 11 (27%) STEMI( ) OMI met the surrogate criteria requiring an acute culprit lesion with TIMI flow of 3 but with highly elevated troponin T > 1.0 ng/mL.Interventions

The STEMI(+) and STEMI( ) OMI groups were treated with similar medications including aspirin (99% and 100%), P2Y12 inhibitors (91% and 83%), nitroglycerin infusion (21% and 27%), and unfractionated heparin infusion (70% and 68%). The STEMI( ) OMI group had the highest rates of precatheterization opioid administration (29.3%) and vasopressor use (19.5%) of all 8 groups studied; however, these were not statistically different from the STEMI(+) OMI group (29.3% vs. 17.9%; p = 0.1683 and 19.5% vs. 13.4%; p = 0.40). All 67 patients with STEMI(+) OMI and 40 of 41 STEMI( ) OMIs had catheterization performed during the index hospitalization. Median time from arrival to cardiac catheterization was 41 min (IQR 23 86 min) for the STEMI(+) OMI group compared with 437 min (IQR 85 1590 min) in the STEMI( ) OMI group ($p \leq 0.001$). The STEMI(+) OMI group was significantly more likely than the STEMI( ) OMI group to undergo cardiac catheterization in < 90 min (76% vs. 28%; $p < 0.001$). Figure 6 shows the times from arrival to catheterization for each relevant group.Other Clinical Outcomes

The prevalence of a new or presumed new wall motion abnormality (present in 35% in the no occlusion group) were highly prevalent and not statistically different between the STEMI(+) and STEMI( ) OMI groups (86% vs. 75%; p = 0.19). Of 7 potential regional wall motion abnormalities, the STEMI(+) OMI, STEMI( ) OMI, and no occlusion groups had a mean (SD) of 2.76 (1.69), 2.29 (1.66), and 0.62 (1.30) regions affected. The STEMI(+) and STEMI( ) OMI groups had the highest rates of cardiac arrest prior to catheterization (10.4% and 9.8%) among all groups evaluated. Precatheterization cardiac arrest was significantly more frequent in both the STEMI(+) OMI group (p = 0.006) and the STEMI( ) OMI group (p = 0.0326) than in the NOMI group. Only 13 patients (2.8%) suffered in-hospital mortality, including 4 STEMI(+) OMI, 1 STEMI( ) OMI, and 8 no occlusion. The composite outcome of precatheterization cardiac arrest, in-hospital mortality, or survival with discharge to hospice was present in 18%, 15%, and 6% of the STEMI(+) OMI, STEMI( ) OMI, and no occlusion groups, respectively.

DISCUSSION

Objections to this new OMI/NOMI classification center around studies that purport to show that early angiography for undifferentiated NSTEMI patients does not

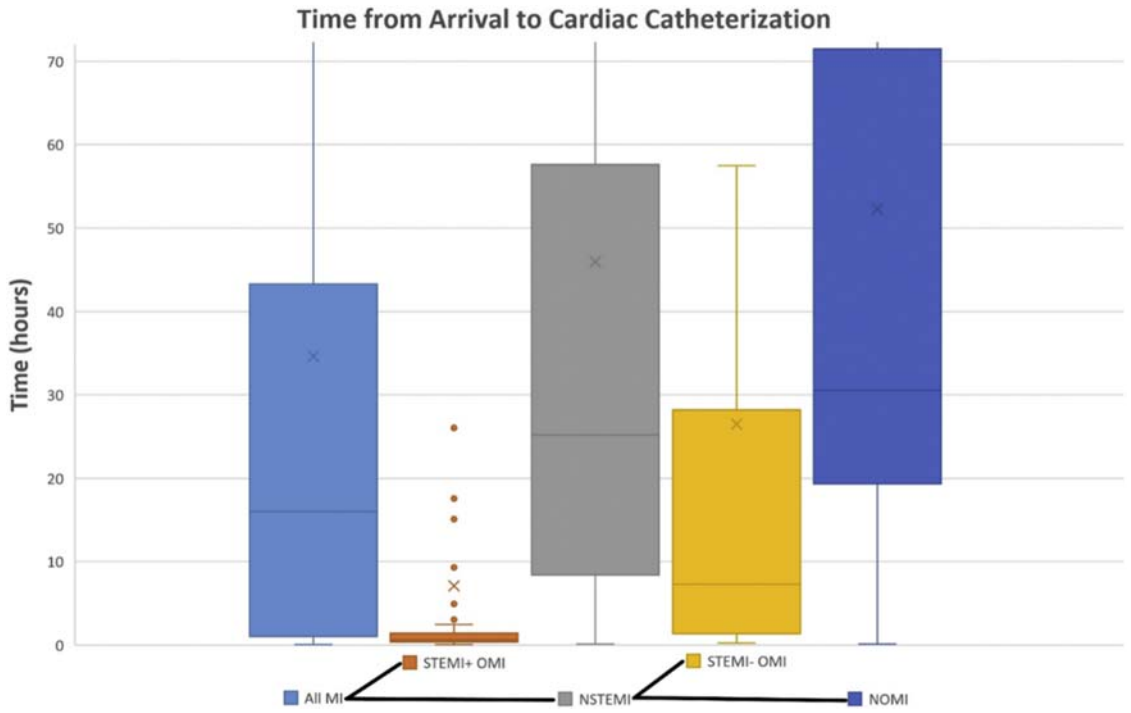

Figure 6. Box and whisker plots showing the distributions of time from arrival to cardiac catheterization among the categories of acute myocardial infarction (MI). The current ST-segment elevation myocardial infarction (STEMI) paradigm is shown, with the non-STEMI (NSTEMI) group additionally broken down into its component subgroups: STEMI(–) occlusion MI (OMI) and nonocclusion MI (NOMI). As a result of our current guidelines, most STEMI(–) OMIs are taken for catheterization within the first few hours, whereas most STEMI(–) OMIs have catheterization delayed well beyond the known benefits of reperfusion from acute coronary occlusion.

result in better outcomes. These objections fail to take into account that these studies excluded patients with persistent symptoms, or did not actually use very early intervention. In the largest such study, patients with persistent symptoms were excluded and "early" angiography was at a mean of 16 h; even so, patients with a GRACE (Global Registry of Acute Coronary Events) score of > 140 did indeed benefit from earlier reperfusion (37 43). In studies that did not exclude patients with persistent symptoms, and patients underwent truly early intervention, outcomes were better (43 45).

Our data support that NSTEMI can be divided into two distinct groups: STEMI( ) OMI and NOMI, and also that STEMI( ) OMI (which are NSTEMI in the current paradigm) are more similar to classic STEMI (STEMI[+] OMI) than to NOMI. Our inclusion criteria yielded a high-risk cohort of suspected ACS patients with a 50.3% rate of AMI and 23% rate of OMI (14% STEMI [+] and 9% STEMI[ ]). We found that only 62% (67 of 108) of OMI presented with formal STEMI criteria (55% [59 of 108] by a second rater), which agrees with the recent study of consecutive chest pain patients by Hillinger et al. in which 60% (81 of 136) of OMI were classified as STEMI by cardiologists who had retrospective access to all patient data including the angiogram (46). In that same study, ECG millimeter criteria only identified 35% of these adjudicated STEMI and only 21% of OMI; this increased to 51% and 30%, respectively, using all serial ECGs.

STEMI( ) OMIs appear to be similar to STEMI(+) OMIs in terms of highly elevated troponins, higher likelihood of, and higher mean number of, wall motion abnormalities when compared with NOMIs. Yet the STEMI( ) OMI group suffered significant delays to catheterization compared with the STEMI(+) OMI group, such that the benefit of reperfusion might have been nullified. It is possible that STEMI( ) OMI would have had significantly better outcomes than STEMI(+) OMI had door to balloon times been equal.

Comparison of Figures 4 and 5 demonstrates the advantage of the OMI/NOMI paradigm over the STEMI/NSTEMI paradigm. Figure 4 viewed alone summarizes our current paradigm and appears at first glance to show that it adequately differentiates AMI patients into two categories (STEMI and NSTEMI), which are distinguished both by the need for emergent intervention and the severity of the AMI (higher peak troponin levels). Figure 5, however, reveals that the NSTEMI group is actually composed of two importantly different groups: STEMI( ) OMI (NSTEMIs with occlusion), who have

angiographic and peak troponin outcomes similar to the STEMI(+) OMI patients; and NOMI (NSTEMI nonocclusions) who have both no occlusive culprit lesion and much less severe MI by troponin. These results support the assertion that occlusion MI (rather than STEMI criteria) may be what truly separates ACS patients into those with emergently salvageable myocardium and those for which emergent invasive intervention is of minimal benefit. These data support further investigation into the potential of the OMI-NOMI paradigm shift. It might be time for our current guideline-recommended paradigm of ACS to be reevaluated with the intent of improving our ability to rapidly recognize OMI to maximize the benefit of emergent reperfusion therapies. Additional research should be directed at identifying ECG, echocardiographic, and other clinical features that can help identify OMI beyond the STEMI criteria.

Limitations

This study is limited by its single-center, retrospective chart review design. We observed few deaths, and we were largely unable to obtain any follow-up data beyond the index visit, which limits our analysis to surrogate markers of patient-centered outcomes in the context of AMI. Fortunately, extensive prior evidence links increasing peak troponin levels with increasing mortality and increased incidence of adverse events and decreased quality of life in survivors (30,33,35,46–48). It is possible that eligible patients with OMI during the study period were missed and not included, such as a patient with unrecognized ACS who was discharged home and did not present again to our institution, or experienced an adverse event outside of our hospital. However, such patients are likely rare and more likely to have been STEMI( ) OMI patients than STEMI(+) (for whom the clear ECG findings would decrease the chances of misdiagnosis). The possibility of missing STEMI( ) OMI patients by our study design likely strengthens rather than weakens our argument that STEMI( ) OMI patients have important rates of adverse outcomes. Next, AMI was not formally adjudicated in our study but was instead collected from the final diagnosis in the medical record; it is possible that there were both missed MIs and non-MI myocardial injury cases or cases of type 2 MI, which received a diagnosis of MI in our data. However, these possible misclassifications do not affect the primary differentiation of OMI from NOMI. Finally, ECG adjudication as STEMI( ) OMI vs. STEMI(+) OMI may have been biased in borderline cases in favor of STEMI( ) OMI. For this reason, a cardiologist blinded to the study goals and hypothesis reviewed all 108 cases of OMI; he classified more cases as STEMI( ) OMI than the first reader, suggesting that the first reader was not biased toward this classification. We used the more conservative reader's classification to protect the study from bias in favor of the OMI-NOMI paradigm. Furthermore, our rate of STEMI(+) OMI (62%) closely matches that of a recent large, prospective study (60%) designed for this purpose by a separate author group (49).

CONCLUSIONS

In this retrospective chart review study of 467 high-risk ACS patients, 40% of OMI did not present with STEMI criteria on ECG. STEMI( ) OMI patients had significant delays to the catheterization laboratory but similarly severe clinical, laboratory, and echocardiographic features as the STEMI(+) OMI group compared with the no occlusion group. These data support the growing notion that STEMI( ) OMI may be an underserved, underidentified, and yet important subgroup of ACS patients who would benefit from emergent intervention, and that classification of AMI by occlusion vs. no occlusion may be more appropriate than classification by ST elevation on the ECG.

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ARTICLE SUMMARY

1. Why is this topic important?

The current guideline-recommended strategy for identifying patients with acute occlusion myocardial infarction (OMI) who will benefit from emergent reperfusion therapy is the ST-elevation myocardial infarction (STEMI) vs. non-STEMI (NSTEMI) paradigm. Because NSTEMI may be OMI or nonocclusion MI, the STEMI/NSTEMI paradigm results in classification of many OMI as NSTEMI, and thus these patients do not receive rapid reperfusion.

2. What does this study attempt to show?

We hypothesized that STEMI(–) OMI would have characteristics similar to STEMI(+) OMI but longer time to catheterization.

3. What are the key findings?

STEMI(–) OMI patients had significant delays to catheterization but adverse outcomes more similar to STEMI(+) OMI than those with no occlusion.

4. How is patient care impacted?

A paradigm shift to recognize electrocardiograms that represent acute coronary occlusion without meeting STEMI criteria can lead to earlier interventions in patients presented to the emergency department with acute coronary syndrome.