8-15-2021

Does Transitioning to an OMI/NOMI Model for the Evaluation of Acute Coronary Syndrome in Adult Emergency Department Patients Improve Outcomes Compared to Contemporary STEMI/ NSTEMI Model?

Ismar Terzic

Does Transitioning to an OMI/NOMI Model for the Evaluation of Acute Coronary Syndrome in Adult Emergency Department Patients Improve Outcomes Compared to Contemporary STEMI/NSTEMI Model?

By

Ismar Terzic, PA-S2

Eric Van Hecke, PA-C, EMCAQ

Paper Submitted in Partial Fulfillment

Of the Requirements for the Degree

Of Master of Science

Physician Assistant Studies

Augsburg University

Date August 15th, 2021

Table of Contents

Abstract……...3

Introduction……4

Background……..……..6

Current ACS Classification/Management……..….6

Historical Context of STEMI/NSTEMI Paradigm Development……..9

STEMI/NSTEMI Paradigm is Inaccurate and Detrimental……12

STEMI Paradigm Undermines Progress……...16

OMI/NOMI Paradigm……...……..19

Methods…….……24

Discussion…….25

Shortfalls of STEMI/NSTEMI……25

OMI/NOMI as a Better Paradigm……...27

Limitations……28

Conclusion……29

References……..…31

Appendix……...……38

Abstract

Acute coronary syndrome (ACS) continues to be the most common cause of death in the United States, and nearly every 34 seconds one American has a coronary event. Based on 12-lead electrocardiogram (ECG) findings myocardial infarction (MI) patients are treated, according to guidelines, emergently with reperfusion therapy if presenting with ST elevation myocardial infarction (STEMI), versus delayed revascularization if presenting with non-ST elevation myocardial infarction (NSTEMI). However, the evidence shows there is a lack of recognition of which patients require immediate catherization utilizing the current guidelines. In recent years, approximately 70% of acute MI (AMI) patients are classified as NSTEMI. Furthermore, it has been observed that approximately 30% of NSTEMI patients have total occluded coronary arteries (TOCA) on angiography yet face a delayed intervention approach that contributes to worsened clinical outcomes.

The current STEMI/NSTEMI paradigm lacks the accuracy in triaging patients who have a suspected acute coronary occlusion (ACO) or near occlusion, with insufficient collateral circulation, whose myocardium is at imminent risk of irreversible infarction without immediate reperfusion. A more recent emerging paradigm to determine who warrants immediate reperfusion is ACO-MI/Non-ACO-MI or Occlusion Myocardial Infarction (OMI) versus Non-Occlusion Myocardial Infarction (NOMI) for short. To answer whether the OMI/NOMI paradigm was superior to STEMI/NSTEMI in evaluating ACS patients, a literature review was conducted primarily utilizing the database PubMed, and certain full-text articles were obtained through Augsburg University's interlibrary loan system. Overall, literature shows limitations of the current STEMI/NSTEMI paradigm and shows that OMI/NOMI paradigm has superior diagnostic accuracy and earlier recognition abilities for treating patients that present with ACS.

Introduction

Acute coronary syndrome (ACS) continues to be the leading cause of death in Americans with a coronary event occurring every 34 seconds [1]. The diagnosis and management of suspected ACS patients is done through primarily risk stratifying according to ECG findings showing either ST segment elevations (STEMI), or non-ST segment elevations (NSTEMI) to determine use of early invasive management or early conservative strategy. In addition to ECG findings, history of presenting symptoms and biochemical markers of myocardial necrosis are also utilized to further classify suspected ACS patients. The current STEMI/NSTEMI paradigm in treating presentations of ACS can be traced back to the early 2000s, in part due to research revealing that the subset of patients presenting with ST elevations on their ECGs had mortality benefits versus those who did not show ST segment elevations when given thrombolytics [2]. Although the research should have been taken as an initial step into risk stratifying patients to determine use of emergent reperfusion therapy, the outcome was an almost synonymous association between the surrogate ECG marker of STE and acute coronary occlusions (ACO). Historically, the STEMI/NSTEMI guideline's development and refinement have been done through flawed methodology, failing to utilize angiographic evidence to accurately determine which patients had occluded arteries with imminent irreversible myocardial damage requiring emergent reperfusion therapy [2-4]. With the current paradigm, the guidelines advocate for patients presenting with NSTEMI to primarily await delayed angiography and only seek emergent (<2 h) reperfusion therapy if deemed high-risk [5]. Approximately 30% of patients that fit NSTEMI criteria have unrecognized total occluded coronary arteries (TOCA) on delayed angiogram [6-7]. The delay in diagnosis and treatment results in increased morbidity, short-, and long-term mortality of patients. Furthermore, there is an increasing incidence of NSTEMI being

recorded worldwide and in recent years approximately 70% of AMI patients are classified as NSTEMI [8-9]. However, STEMI criteria have a limited diagnostic accuracy, missing nearly one-third of ACO, and causing a substantial amount of false catherization laboratory activations [10]. In addition, our understanding of ECG changes indicative of ACO have expanded and include minor STE not fulfilling STEMI criteria, STE disproportionate to preceding QRS, unusual patterns with contiguous leads showing opposite ST deviations, and some patterns not showing STE at all. Attempts at integrating these other ECG findings indicative of ACO into terms such as “STEMI equivalents”, fail at gaining widespread understanding.

For reasons outlined above, a gap in treating NSTEMI patients with ACO clearly exists, and thus a call for a paradigm shift to change the dichotomization of ACS into a more direct pathological understanding has been proposed. The proposed alternative paradigm to STEMI/NSTEMI is ACO-MI/non-ACO-MI or Occlusion Myocardial infarction (OMI) versus Non-Occlusion Myocardial Infarction (NOMI) for short. Simply put, do they present with occluded or near occluded coronary arteries with imminent myocardial damage requiring immediate intervention or not. By changing the paradigm to OMI/NOMI, diagnosis does not solely rely on ECG findings, which can be inconclusive, but includes clinical suspicion, ongoing symptoms, biomarker elevation, echocardiography, computed tomography, and conventional angiography. It is hypothesized that by transitioning to OMI/NOMI model for the evaluation of acute coronary syndrome in adult emergency department patients results in improved outcomes compared to the contemporary STEMI/NSTEMI paradigm. Objectives of this paper include outlining current ACS management, the limitations and historical development of STEMI/NSTEMI, and present the OMI/NOMI model and analyze how it compares.

Background

Current ACS Classification/Management

When discussing suspicion for acute myocardial ischemia or infarction (AMI) an umbrella term of acute coronary syndromes (ACS) is traditionally utilized. Under the current classification system of ACS refers to one of three clinical syndromes: unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), or ST-segment elevation myocardial infarction (STEMI). The leading symptom in patients suspected of ACS is acute chest discomfort described as pain, pressure, tightness, and burning [5]. In addition, symptoms can include dyspnea, epigastric pain, and radiating pain. Suspected ACS patients ideally undergo a baseline resting ECG within 10 minutes of presentation two differentiate two types of patients with risk of myocardial infarction. Based on 12-lead ECG findings, patients are assigned to STEMI, if ST segment elevation is noted and are recommended to undergo immediate reperfusion by primary percutaneous coronary intervention (PCI) (door-to-balloon time within 90 minutes), or fibrinolytic therapy if PCI is not available [11]. Patients with acute chest pain discomfort but no persistent ST elevated ECG are termed NSTEMI or UA, until positive serial cardiac markers rule in NSTEMI and rule out UA. NSTEMI patients are to undergo immediate invasive strategy (<2 hrs) only if deemed high-risk, which can be characterized by recurrent or ongoing chest pain, marked ST-segment depression on 12-lead ECG, heart failure, and hemodynamic or electrical instability regardless of ECG or biomarker findings. Conventional teaching is that STEMI is generally regarded as reflecting an acute total or subtotal coronary occlusion completely interrupting blood supply and causing transmural ischemia. While NSTEMI is considered cardiomyocyte necrosis due to acute partial occlusion of a coronary vessel causing incomplete interruption of blood supply causing non-transmural (subendocardial)

ischemia. However, it has been observed that totally occluded coronary arteries (TOCA) occurs among NSTEMI patients as well, and two recent meta-analyses reported approximately 30% of the patients diagnosed with NSTEMI had TOCA [7,12-13].

The diagnosis of AMI, (cardiomyocyte necrosis), in a clinical setting consistent with myocardial ischemia, is met when the following criteria are met; detection of an increase and/or decrease of a cardiac biomarker, preferably high-sensitivity cardiac troponin (hs-cTn) T or I, with at least one value above the 99th percentile of the upper reference limit and at least one of the following: 1. Symptoms of myocardial ischemia. 2. New ischemic ECG changes. 3. Development of pathological Q waves on ECG. 4. Imaging evidence of loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology. 5. Intracoronary thrombus detected on angiography or autopsy [11].

The increased access to high sensitivity troponin assays has led to an increased incidence rate of NSTEMI being recorded worldwide, as well as, nearly 70% of AMI patients being classified as NSTEMI in the United States [8-9]. Several definitions of AMI based upon assumed cause exist, the most common being Type 1 MI, which is characterized by atherosclerotic plaque disruption that results in intraluminal thrombus formation that impedes myocardial blood flow leading to myocardial necrosis. Type 2 MI is a consequence of mismatch between oxygen demand and oxygen supply that is caused by a condition other than plaque instability. Type 2 MI etiologies include hypotension, hypertension, tachyarrhythmias, bradyarrhythmias, anemia, hypoxemia, coronary artery spasm, spontaneous coronary artery dissection, coronary embolism, and coronary microvascular dysfunction. Most Type 1 and Type 2 etiologies present as NSTEMI, however, can present as STEMI as well [14]. Type 3 MI involves patients with unexpected death before biomarkers are drawn or appear in the blood.

Type 4 MI is associated with percutaneous coronary intervention (PCI). Finally, type 5 MI is from coronary artery bypass graft surgery (CABG).

It is generally understood that invasive revascularization interventions are most useful in a Type 1 MI etiology. To maximize benefits of such interventions, deciding whether it should be done immediately/emergent (within 2 h), early (within 24 h), or delayed (within 25-72 h), and the selection of approach (PCI or coronary artery bypass grafting (CABG) need to be made as early as possible. Angiographic evidence is utilized to classify coronary artery patency using the TIMI Grade Flow scoring system. Grade 3 is normal flow with full perfusion, Grade 2 is delayed flow with full perfusion, Grade 1 is penetration without distal perfusion, Grade 0 is complete occlusion. It is the patients that have either a full occlusion, or near-occlusion with insufficient collateral circulation with imminent risk of irreversible infarction that benefit from emergent reperfusion therapy. Those whose myocardium is at risk, but not imminently, can be managed with medical therapy including antiplatelets, anticoagulants, and/or delayed reperfusion.

Contemporary triage risk scores are utilized in identifying higher-risk patients that present with ACS to aid in risk stratification. The TIMI (Thrombolysis in Myocardial Infarction) score estimates adverse outcomes in patients with unstable angina or NSTEMI but can also be used to risk stratify patients with presumed ischemic chest pain. Similarly, the GRACE (Global Registry of Acute Coronary Events), estimates in-hospital, and 6-month to 3-year mortality in patients with known STEMI, unstable angina/NSTEMI to determine morality risk and guide more appropriate interventions. However, studies suggest neither TIMI risk score nor GRACE risk scores can very accurately identity which patients' angina symptoms are due to ACS, and can only modestly identify NSTEMI patients with underlying TOCA who are at higher risk [7,13,15]. Guideline's recommendation of delayed reperfusion in NSTEMI patients results in a

mean time to angiography or PCI being more than 24 h [7,13]. Emergent reperfusion is recommended if NSTEMI patient is deemed high-risk, characterized by recurrent or ongoing chest pain, marked ST-segment depression on 12-lead ECG, heart failure, and hemodynamic or electrical instability regardless of ECG or biomarker findings. There is also no difference in time to angiography or PCI between NSTEMI patients with or without TOCA [13].

Historical Context of STEMI/NSTEMI Paradigm Development

Before the reperfusion era ushered in the STEMI/NSTEMI paradigm, the first established MI paradigm was Q-wave/non-Q-wave MI dichotomy [16]. Retrospectively classifying patients based on Q wave development on ECG, or sign of irreversible transmural loss of myocardium, was the best available knowledge for the better part of the 20th century. The historical timeline of major events providing insights into the pathogenesis and management of AMI leading up to the reperfusion era is presented **Fig. 1** [17]. The 1980s and early 1990s were defined by landmark trials and meta-analyses showing IV fibrinolytics had substantial survival benefits and outcomes for suspected ACS patients, especially when given early [2,18,19].

The randomized control studies evaluating fibrinolytics use in patients presenting with AMI began to shift our paradigm from retrospective diagnosis and seldom treatment options, but rather towards prospective identification and treatment. The 1994 Fibrinolytic Therapy Trialists' (FTT) meta-analysis pooled data from 58,600 patients enrolled in 9 randomized control studies using highly suspicious patients presenting with acute chest pain that were randomized to either thrombolytics or placebo [2]. The average number of patients needed to treat to benefit one of the patients expressed as NNT, was 56 from lytics compared to placebo, showing a significant mortality benefit before performing any subgroup analysis. Subset analysis of the groups from the RCTs was done to determine which groups had the highest benefit or harms. The subgroups

were defined vaguely by ECG findings of "ST elevation (STE)", "ST depression (STD)", or "Normal". Only five of the RCTs had defined their version of STE, which had varying cutoffs and methods of measurement. The definition of "Normal" and "STD" were not adequately defined either. The remaining four of the nine trials did not use ECG for enrollment. Upon subset analysis, STE was found to be the most closely associated ECG finding as an arbiter of fibrinolytic administration which improved NNT for short term mortality from 56 to 43. On the other hand, those subset groups defined as "Normal" or "STD" showed a non-significant trend towards mortality harm expressed as number needed to harm (NNH), (NNH=143, 42). The meta-analysis helped identify that the poorly defined "STE" can be used as surrogate marker to predict potential acute coronary occlusion (ACO) and thus mortality benefit from lytics than not looking at the ECG at all. The meta-analysis did not use angiographic findings to identify which patients had an ACO. In 2000, the ACC/AHA guidelines formally changed the paradigm from Q-wave vs. non-Q wave MI to STEMI vs NSTEMI [20].

Research continued focusing on delineating what appropriate amount of STE was deemed a STEMI and fine tuning it, but often failing to utilize angiographic evidence to determine who indeed had an ACO. Menown et al., utilized ECG and biomarker findings using 1,190 subjects to determine that ≥ 2 STE in at least one of the anteroseptal leads, or ≥1mm in any of the other leads which had a 56% sensitivity and 94% specificity for AMI vs no AMI [3]. The study did correctly classify 83% of patients as having AMI, however not utilizing angiography means patients without occlusion were included. The results suggest the approach can predict AMI accurately, but the same cannot hold true for predicting ACO. The result of the study instituted the First Universal Definition of MI and the first STEMI criteria findings: patients with STE that had new or presumed new ST segment elevation in two or more contiguous leads with

≥0.2 mV in leads V1, V2, or V3, or ≥0.1 mV in other leads. Patients without STE could have findings indicative of ischemia that could progress to MI were STD, or T-wave abnormalities that should be observed in two or more contiguous leads, or symmetric inversion of T waves ≥1mm in at least two contiguous leads [21]. Subsequent studies by Mcfarlane et al. and Wu et al., found that ironically baseline STE was a common appearance among apparently healthy adults who presumably did not have ACO [4,22]. Wu et al. even found that 2% of Chinese males aged 18-40 had 3mm or more of J point elevation in V1 and V2 at baseline, which is at odds of the first universal definition of MI [22]. Regardless, in 2004 the ACC/AHA recommended that STE of ≥1mm in any two contiguous leads or adjacent limb leads warranted fibrinolytic therapy with symptom onset within the prior 12 hours [23].

The Second Universal Definition of MI came about in 2007 after research showed that implementing sex-based cutoffs for STEMI criteria would increase the sensitivity and specificity of correlating ECG findings to elevated biomarkers [24-25]. The Second Universal Definition recommended two contiguous leads with at least 1.0mm STE, except for leads V2-V3 which requires 1.5mm in women and 2.0mm in men [25]. The definition was primarily based on what Macfarlane et al. had found performing a logistic regression technique to revise the STEMI criteria based on age and sex-based cutoffs, which increased sensitivity from 42% to 47% and specificity from 96% to 99% when correlating the ECG findings to biomarker elevation [24]. No angiographic evidence was utilized, so data on ACO patients was not reported.

In 2009, the current STEMI criteria were introduced with both age and sex-based cutoffs for STE being, new ST-elevation at the J-point in 2 contiguous leads with the cut-point: ≥1 mm in all leads other than leads V_2–V_3 where the following cut-points apply: ≥2 mm in men ≥40 years; ≥2.5 mm in men <40 years, or ≥1.5 mm in women regardless of age [26]. For STD and T-

wave changes new horizontal or downsloping ST-depression ≥0.5 mm in 2 contiguous leads and/or T inversion >1 mm in two contiguous leads with prominent R wave or R/S ratio >1 were defined. These criteria were subsequently included into the 2012 development of the Third Universal Definition of MI, with the addition of some minor reference that other ECG findings like hyperacute T-waves can possibly represent AMI [27]. The ST-elevation criteria have continued to be included in even the most recent 2018 fourth universal definition of MI [28]. STEMI criteria has become the guideline-based approach to diagnosing ACO with a notion that it is the most accurate marker for determining ACO, and thus a marker for who needs emergent reperfusion therapy.

STEMI/NSTEMI Paradigm is Inaccurate and Detrimental

Just as Q-wave/non-Q wave served as a surrogate ECG marker for MI previously, STEMI/NSTEMI is currently serving that identical purpose as a marker of acute coronary occlusion that fails to account for the underlying pathology. Keeping the underlying pathology in mind, STEMI criteria fails to identify acute coronary occlusion accurately.

Schmitt et al. was one of the first to find the limitations of utilizing STEMI criteria [29]. A total of 1,788 patients with suspected AMI based on clinical symptoms and positive CK-MB, were prospectively enrolled for emergent coronary angiography. In total 23% had confirmed ACO (418/1788), and out of those 418 patients, 29% did not meet STEMI criteria. The least sensitive measure of STEMI criteria was in those presenting with an acute left circumflex occlusion which had a high miss rate of 50%. The PARAGON-B trial was a randomized control study using 1,957 patients with non-STE ACS presentation [30]. It was found that 27% of those patients had completely occluded culprit vessels on next day angiography. In addition, it was found that these patients had larger infarcts (median peak creatine kinase–MB 4.3 vs 2.1 × upper

limit of normal, $P < .0001$) and higher risk adjusted 6-month mortality (hazard ratio 1.72, 95% CI 1.07-2.79) despite similar in hospital treatment. Similar findings were found in the TRITON-TIMI-38 randomized control trial for patients undergoing cardiac catherization, in which 26.2% had completely occluded culprit arteries at the time of catherization [31]. Additionally, 48.4% of those with occlusion, the culprit artery was the left circumflex. The 30-day incidence of composite of death and MI was significantly higher in the occluded artery group and the median time from ECG to PCI was 29.4 hours. Khan et al., performed a meta-analysis from seven studies in which NSTEMI patients were prospectively enrolled and assessed for occluded culprit arteries [32]. Out of 40,777 NSTEMI patients, 10,415 (25.5%) had total occluded coronary arteries (TOCA) found on angiography an average of 24 hours after presentation. Furthermore, these unrecognized ACO patients had increased risk of both MACE (major adverse cardiovascular events) in the short and medium to long term, and all-cause mortality.

Overall, NSTEMI patients with unrecognized ACO face adverse cardiovascular events. Even the most recent publications show that NSTEMI with ACO compared to NSTEMI without ACO have increased mortality ratios, increased re-infarction rates, and increased mortality in the short and long term [7,13]. The authors concluded better risk stratification tools are needed to facilitate earlier revascularization and improving outcomes in NSTEMI patients with ACO, because of the increased risks associated with missing the diagnosis [13].

Studies highlight a substantial amount of ACO patients present with subtle STE not fulfilling current STEMI criteria. One study found that patients with angiographic evident ACO presenting with subtle STE of (.1-1mm), 18.3% had not even a single lead with 1mm STE [33]. Despite having smaller infarcts, the subtle STE subgroup had more frequent multivessel disease, larger delays to reperfusion, and was not associated with better outcomes. Smith et al.,

retrospectively compared 143 subtle proven acute left anterior descending (LAD) occlusions and found that 22% of patients (33) that had subtle LAD occlusion with a mean STE ≤1mm, 19 patients with no leads showing more than 1mm, and 8 patients with less than or equal to 1mm in only 1 lead [34]. AM et al., analyzed 1,500 consecutive patients with angiographic complete or near occlusion to determine if through re-reading their ECG they would meet STEMI criteria [35]. Surprisingly, even with the bias of knowing these patients had ACO in addition to using a more liberal cutoff of ≥ 1mm STE in any 2 contiguous leads, 28% (423) patients still did not meet the criteria.

Another failure of utilizing STEMI ECG criteria is that it has poor accuracy among clinicians and has poor interrater reliability for detecting ACO. McCabe et al., performed a cross sectional survey using EM physicians and cardiologists to review 36 ECG for prospective STEMI activation [36]. 24 of the ECGs were true positives (STEMI), while 12 of the cases had no culprit lesion (no STEMI). Physicians were asked "based on the ECG above, is there a blocked coronary artery present causing a STEMI?". 124 physicians interpreted a total of 4,392 ECGs and showed that intrareader agreement (kappa) for ECG interpretation was 0.33, reflecting poor agreement. Sensitivity to identify true STEMIs was 65% and specificity was 79% [36]. Interesting enough, even after adjusting for experience there was no difference in the odds of overall accurate interpretation between specialties [36]. Other studies have also showed poor interrater reliability and wide variations among experienced electrocardiographs in determining which ECGs had STE with need for PCI from nonischemic STE [37-38]. Carley et al. showed that even among physicians that commonly prescribe thrombolysis the observed STE magnitude varied, because doctors use a wide variety of points on the ST segment to assess elevation [39].

Most recently prospective cardiologist subjective evaluation revealed only 49% sensitivity for predicting ACO [40].

In addition to failing to identify ACO, STEMI criteria leads to many false STEMI activations. In one study out of 411 STEMI activations by EM physicians, 146 (36%) were deemed false positive that did not warrant PCI [41]. In another study using 1,335 patients from 31 regional hospitals in Minnesota who presented with suspected STEMI and underwent angiography, 187 (14%) did not have a clear culprit coronary artery, 9.5% did not have significant coronary artery disease, and 11.2% had negative biomarkers [42].

The development of computerized diagnostic algorithms to assist in the interpretation of ECG has been used in suggesting STEMI, but the research shows that even automated interpretation has high rates of error [43-45]. The algorithms have a wide variation of false positives (0-42%), and false negative results (22-24%). Hillinger et al., in a prospective validation of current ECG criteria reported recently that sensitivity of computer algorithm measurement was 21%, and for cardiologist-adjudicated STEMI was still remarkably low (35%) [40]. The recommendation is that computer-assisted ECG interpretation should not be used as a sole means to diagnose STEMI, but it still can bias physician judgement [46-47]. Furthermore, computer interpretation basis is on STEMI criteria and can miss the subtle ST elevation, (which may be significant in small amplitude QRS complexes), ST depression in aVL (which is sensitive for inferior MI), and subtle signs of LAD occlusion like terminal QRS distortion [48]. Finally, if the computer interpretation reads “normal” it must be carefully interpreted because it can miss the ischemic morphology (straight or convex ST segments, terminal T wave inversion, down-up T waves, hyperacute T waves, and inverted U waves), and dynamic changes (subtle changes, pseudonormalization of ST segments, or T-waves) [48-49].

STEMI Paradigm Misses Other Findings

The final point towards why STEMI/NSTEMI fails as a paradigm for ACO is that it acts as a cognitive roadblock. The words STEMI make one cognitively assume that STE is the only ECG variable that matters, missing other subtleties of ECG interpretation [50]. For example, proportionality of STE, STD, or T-wave size must be assessed relative to the QRS amplitude, which is absent from STEMI/NSTEMI criteria [51]. With lower QRS voltage, the more significant any STE/STD/T-wave size becomes.

Rules for determining subtle left anterior descending (LAD) coronary occlusion over normal variant STE have been found to be very accurate utilizing a four variable formula resulting in sensitivity of 86% and specificity of 92% for LAD occlusion [52]. Normal variant STE is also shown to present with an S-wave or a prominent J-wave notch in both V2 and V3, and absence of it is termed “terminal QRS distortion” seen only in LAD-ACO with a 100% specificity [53]. In subtle inferior STE, looking at aVL, which is the only lead that is truly opponent the inferior wall, and finding evidence of any STD is a sensitive, early sign of inferior ACO [54-55].

STE due to secondary repolarization abnormalities have also been evaluated for more diagnostic ECG findings of ACO. For example, modified Sgarbossa criteria have been evaluated to accurately diagnose ACO in presence of left bundle branch block (LBBB) (sensitivity=91%, specificity 90%), or ventricular paced rhythm (sensitivity=67%, specificity 99%) [56-57]. It has been shown that STE >25% of the QRS amplitude can specifically be used for differentiating STE due to ACO from STE due to left ventricular hypertrophy with sensitivity 64%, specificity 93% [58]. Rules for differentiating STE from post-MI ventricular aneurysm or pericarditis from ACO have also been published with high sensitivity (91%, 98%) and specificity (81%, 100%)

[59-60]. Shaikh et al., has recently proposed ACS patience presenting with new onset right bundle branch block (RBBB) to potentially be a "STEMI equivalent" finding to indicate acute reperfusion, because of it likely indicating proximal occlusion of the LAD [61].

Notable patterns without contiguous STE can also indicate ACO. Aslanger's pattern may present in about 6.3% of NSTEMI patients and represent approximately 13.3% of inferior ACO, often revealing multivessel disease and resulting in higher mortality risks [62]. Another example of a noncontiguous STE pattern is the recently published South African flag sign, indicative of a diagonal occlusion [63]. Isolated posterior MI is commonly missed due to it not presenting on standard 12 lead ECG with STE, but rather reciprocal changes are seen on anteroseptal leads with STD, which might require additional V7-V9 leads placed on the posterior chest to adequately detect [31]

Dynamic ECG findings not showing any ST deviation can also indicate ACO. Hyperacute T-waves, widely considered a precursor sign of ACO and preceding evolvement to a STEMI pattern, is described as broad-based, asymmetrical, and tall compared with preceding R-wave, most apparent with ACO of the LAD [64]. In addition, de Winter pattern, widely considered a "STEMI equivalent", in part due to its high positive predictive value of ACO, is a form of hyperacute T-wave with ST depression [65]. Wellens syndrome presents as an ECG pattern primarily showing biphasic or deeply inverted T-waves in leads V2-V3 requiring early recognition as it represents a pre-infarction state of the LAD, with previous reports of 75% of patients developing infarction without definitive PCI intervention [66]. Shark fin appearance caused by fusion of QRS, ST-segment, and T waves, is another high-risk pattern reflecting presence of large area of transmural ischemia and predicting significant mortality [67]. Furthermore, serial ECGs obtained over 15-30 minute intervals over the first hour might be

required to capture some of the dynamic changes that occur in an AMI, and has been shown to improve the sensitivity for STEMI and ACS [68]. Other high-risk criteria potentially indicating ACO include (transient STE, poor QRS voltage, resting U wave inversions, multiple leads showing STD and/or significant magnitudes of STD, etc..) summarized in **Table 1** [51]. Images of ECG signs by suspected culprit coronary artery are presented in the appendix (**Fig. 2-Fig. 5**) [51].

ECGs can be inconclusive and utilization of clinical, laboratory, and imaging characteristics to identify high risk NSTEMI patients with ACO can aid in timely definitive treatment. Utilizing data from 17,739 NSTEMI patients with totally occluded coronary arteries revealed approximately 70% were male and a majority were between 58-69 years old [7,13]. Risk factors like hypertension, diabetes mellitus, dyslipidemia, and smoking use were also associated with increased occlusion in NSTEMI patients. Characteristics of chest pain such as severity, duration, number of episodes, and persistence despite medical treatment raise suspicion for ACO as well.

Echocardiograph findings can also aid in determining high risk NSTEMI patients, since changes can present prior to ECG changes or development of symptoms [69]. Regional wall motion abnormalities on echocardiography localize to territories of occluded coronary arteries and can be visualized by abnormalities in segmental motion described as hypokinetic, akinetic, or dyskinetic. Reduced left ventricular ejection fraction, new or worsening mitral regurgitation, and new ventricular septal defects have been recognized as markers of risk severity in NSTEMI patients [5,70]. Determining myocardial strain through speckle-tracking echocardiography has also been used to identify ACO with high accuracy when territorial circumferential strain value was >-10% [71].

Other imaging modalities for NSTEMI patients with possible occlusions include computed tomography (CT) coronary angiography. Results from the follow up study of the VERDICT trial showed CT coronary angiography to be equivalent to invasive coronary angiography in differentiating obstructive and nonobstructive coronary artery disease, thus being a potential timely non-invasive approach to aid in definitive diagnosis [72].

OMI/NOMI Paradigm

A classification system other than STEMI/NSTEMI for ACS has been proposed [73] An accurate proposal is one that considers the pathophysiologic substrate, which would be an acute coronary occlusion MI vs non-acute coronary occlusion MI, or to put it shortly occluded MI vs non-occluded MI (OMI vs NOMI). OMI conceptually equating to an acute coronary occlusion or near occlusion with insufficient collateral circulation, such that downstream myocardium will undergo imminent infarction without emergent reperfusion. NOMI refers to an AMI without angiographic, laboratory, or clinical evidence of OMI, or using the current paradigm, an NSTEMI without occlusion. Utilizing the OMI/NOMI framework does not only limit to ECG interpretations, which can sometimes be nondiagnostic, but also includes diagnosis via biomarkers, echocardiography, computed tomography, and/or conventional angiography [50].

Definitions that come about with introducing the new paradigm whilst including the current guidelines are as follows. STEMI (+) OMI is a true positive STEMI, which means it meets current STEMI criteria and is found to have OMI as the cause of the STE and AMI. STEMI (-) OMI refers to patients that do not meet ECG STEMI criteria but have an occlusion (an NSTEMI with occlusion). False positive STEMI refers to those meeting STEMI criteria, but the STE is not due to ischemia and there is absence of OMI on angiogram. The ACS spectrum

using primarily STEMI/NSTEMI paradigm and OMI/NOMI paradigm are displayed in the appendix (**Fig. 6, Fig. 7**) [74].

Meyers et al., retrospectively reviewed 467 high-risk ACS patients and directly compared STEMI/NSTEMI with the OMI/NOMI paradigm [74]. 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. Out of the 467 high-risk ACS patients 234 had an AMI (50.1%). In total 108 met OMI criteria with 67 being STEMI (+) (62%) and 41 being STEMI (-) (38%). Median peak troponin T between STEMI (+) OMI was similar to STEMI (-) OMI (5.36ng/mL vs. 4.44ng/mL). Rates of new or presumed new wall motion abnormalities was similar as well (86% vs. 75%). A composite outcome of catheterization cardiac arrest, in-hospital mortality, or survival with discharge to hospice was 18% and 15% between STEMI (+) OMI and STEMI (-) OMI. Median time from arrival to cath was delayed in STEMI (-) OMI patients (437 vs. 41 minutes), with only 28% undergoing cath in less than 90 minutes compared to 76% in the STEMI (+) OMI group ($p<0.001$).

Meyers et al., recently performed a retrospective case control study of 808 patients with suspected ACS symptoms and compared structured expert ECG interpretation suggestive of OMI to STEMI criteria for the diagnosis of an OMI [75]. OMI was defined as either an acute culprit artery with TIMI flow of 0-2, or a culprit artery with TIMI flow 3 with peak troponin T ≥1.0 ng/mL or I ≥10.0 ng/mL. The expert ECG findings considered these 8 other findings highly suggestive of OMI, "subtle STE not meeting criteria, hyperacute T waves (including de Winter pattern), reciprocal ST depression and/or negative hyperacute T waves, STD maximal in V1-V4 indicative of posterior OMI, suspected acute pathologic Q waves (meaning Q waves associated with subtle STE which cannot be attributed to old MI), terminal QRS distortion (absence of S-wave preceding any subtle STE, where an S-wave would be expected), any STE in

inferior leads with any STD or T wave inversion in lead aVL, and positive modified Sgarbossa criteria (MSC) for a patient with left bundle branch block (LBBB) or ventricular paced rhythm (VPR)" . In total 49% had an AMI with 265 (33%) having an OMI, and only 41% of total OMI patients meeting STEMI criteria. The results showed higher sensitivity, and similar specificity using OMI criteria compared to STEMI criteria among the two interpreters (Interpreter 1 sensitivity 86% vs 41%, specificity 91% vs 94%), (Interpreter 2 sensitivity 80% vs 36%, specificity 92% vs 91%). Inter-rater reliability was high between interpreters with a 97.2% (kappa value of 0.893) for determining STEMI criteria and 94% agreement for the diagnosis of OMI (kappa value of .849). OMI criteria lead to correctly identifying 146 (55%) of OMI patients an average of 3 hours and median of 1.5 hours earlier than using STEMI criteria. Out of the 146 patients with OMI, 120 never met STEMI criteria on any serial ECG recordings. Most common OMI ECG findings were subtle STE not meeting STEMI criteria (83%) and reciprocal ST depression and/or reciprocal T-wave inversion (82%). The STEMI (-) OMI patients had similar infarct sizes as STEMI (+) OMI patients (average peak TnT ng/mL 5.29 vs 6.06) but had greater delays to angiography with average time to cath (1,181 minutes vs. 265 minutes) and less undergoing cath <90 minutes from presentation (38% vs. 71%).

The DIFOCCULT study also compared the OMI/NOMI approach versus STEMI/NSTEMI and was the largest designed study to date challenging the current paradigm [10]. It was a single center, retrospective case control study of adult patients presenting to the emergency department clinically for ACS at a tertiary care center for PCI in Turkey. Utilizing the fourth universal definition of MI, the three groups were STEMI, NSTEMI, Control (ACS excluded). ACO was defined by total occlusion or presence of culprit lesion on angiography with peak troponins I level equal to or greater than 1.0ng/ml + an at least 20% rise within 24 hours, a

highly elevated peak troponin (greater than 5.0 ng/ml), or cardiac arrest before any troponin rise has been documented with supporting clinical evidence of possible ACO. The study ruled out 15,510 ACS patients by serial troponin, and had 1,152 patients with STEMI, 2,352 with NSTEMI. Using 1,000 patients for each group analysis, those initially classified as having NSTEMI, 282 (28.2%) were re-classified by ECG reviewers as having OMI due to minor STE with reciprocal STD (215), hyperacute T waves or de Winter's patterns (35), subtle anterior STE (18), nonconsecutive STE (14). Inter-observer agreement was high for detecting these subtle ECGs (kappa=0.834). Reclassified NSTEMI had a frequency of ACO of 60.9%, while the frequency of ACO in STEMI was 85.3%. Myocardial damage by 24 to 48 hour troponin I measure showed reclassified NSTEMI had (5.703ng/ml), STEMI: (32.990 ng/ml), non-reclassified NSTEMI: (0.622ng/ml). Mortality rates were similar between reclassified NSTEMI and STEMI in hospital (5.0% vs. 8.3%), and long-term (10.6% vs. 13.7%). In terms of diagnostic accuracy for ACO after weighted values corrected for real admission rates of each group the OMI/NOMI approach was overall superior to STEMI/NSTEMI with sensitivity (67.9% vs. 54.4%), specificity (96.7% vs. 99.0%), positive predictive value (68.2 vs. 43.4), and negative predictive value (96.6 vs. 94.9). In addition, accuracy for long term mortality weighted was also shown to be overall higher using the OMI/NOMI approach compared to STEMI/NSTEMI with sensitivity (64.6% vs. 50.4%), specificity (91.4% vs. 88.8%), positive predictive value (11.4 vs. 7.1), and negative predictive value (99.3 vs. 99.1). In this study, 17.9% of ACO in the NSTEMI group were still missed.

Implementing teaching of more subtle ECG findings included under the OMI/NOMI paradigm has been successfully done and has even lead to outcome improvement. A recent multi-centre quality improvement initiative to educate emergency physicians on OMI ECG

findings was done to reduce diagnostic time for patients presenting with ACO [48]. First emergency department ECG to the time a Code STEMI was activated, or ECG-to-Activation (ETA) time, was measured to reflect emergency physician clinical decision making. Also, percentage of Code STEMIs without culprit lesions was measured. Education was primarily done through weekly web-based feedback on unnecessary cath lab activations and on STEMI-equivalents/subtle occlusion findings. ETA time was reduced by 20 minutes, from 28.0 (95% confidence interval [CI] 15.0–45.0) to 8.0 (95% CI 6.0–15.0), which is clinically significant, and was done without increasing the percentage of Code STEMIs without culprit lesions; baseline of 28.2% (95% confidence interval [CI] 17.8 to 38.6) and interventional period 20.0% (95% CI 11.2 to 28.8). The most common improvement in ECG diagnosis of ACO was subtle LAD occlusion (e.g. borderline anterior ST elevation with convex ST segments, hyperacute T waves or reciprocal changes), subtle inferior MI (minor inferior ST elevation with reciprocal ST depression in aVL), and posterior MI (anterior ST depression with minor posterior ST elevation).

Methods

Literature review was first conducted utilizing Dr. Smith's ECG Blog, under which OMI relevant literature is compiled. Meyers and Smith's "OMI Manifesto" served as the initial principal source for journal articles relevant to STEMI/NSTEMI and OMI/NOMI literature. Independent review of the cited literature was performed. Personal analysis of original studies allowed for deeper understanding and verification of material accuracy. In addition, literature searches were conducted primarily using PubMed literature database and Google Scholar. Keywords for searches included "ACS", "STEMI vs NSTEMI", "STEMI", "NSTEMI", "OMI vs NOMI", "OMI", "NOMI" were performed. Articles that were relevant to the thesis topic were reviewed and included. Searches were limited to articles in which access to full texts could be obtained. The Augsburg University's Lindell Library interlibrary loan was utilized to obtain some articles. Figures and tables from several articles that were found useful were included in the Appendix.

Discussion

The objective of this paper was to conduct an evaluation of the current AMI paradigm STEMI/NSTEMI and compare it to the newly emerging paradigm OMI/NOMI for evaluation of patients presenting with ACS to determine whether a new paradigm would result in better outcomes. Although the research is still limited, there are several findings that ultimately point towards the benefits of using the OMI/NOMI paradigm.

Shortfalls of STEMI/NSTEMI

When examining the historical development of STEMI/NSTEMI criteria to diagnose ACO there is clearly poor methodology that has led to the adoption of it into current guidelines. Ushering in the era of reperfusion therapy in part due to placebo-controlled trials utilizing thrombolytics, without subset analysis, showed that patients benefited when presenting with symptoms associated with ACS. ECGs were used to further analyze who would benefit the most from lytics, however, in the meta-analyses the definitions of "STE", "STD", and "normal" were poorly defined and varied substantially between the RCTs [2]. In addition to poorly defined metrics, the lack of angiography evidence of ACO in the studies did not prove if in fact STE patients, who were shown to have decreased mortality with thrombolytics, had pathology warranting emergent reperfusion. The results do suggest that overall, the STE subgroup likely had more ACO patients, thus benefiting more from thrombolytics, but still neglects false positives in the group and false negatives in the non-STE group. The studies showing thrombolytics are beneficial in AMI patients should have been taken as mere beginning to risk stratifying ACO patients, but instead led to STEMI being synonymous with ACO requiring emergent reperfusion therapy. Research refining STE criteria was also done without proper methodology incorporating angiographic evidence of occlusions, but rather dependent on

biomarker positivity, which lacks sensitivity for ACO. Evaluating the historical research revealed that AMI diagnosed by biomarkers is the outcome that was utilized to determine ECG findings and fine tune STEMI criteria, disregarding any other potential ECG findings of ACO in the process. Using angiographic evidence to correlate with ECG findings would have been a better approach in assessing patients presenting with ACO, because then determining who would benefit most from emergent reperfusion therapy could be made.

When examining the accuracy of STEMI/NSTEMI for discovering ACO, the evidence shows that it misses approximately 25-30% of ACO in NSTEMI presenting patients, and sometimes even as high as 50% in ECG silent coronary arteries like the Left circumflex [6, 29]. STEMI criteria results in almost 14-36% of false cath lab activations in patients that are found to not have culprit lesions [41-42]. With patients that undergo false positive activation the risks outweigh the benefits, with possible exposure to complications of coronary angiography including coronary dissections, perforations, early diagnostic closure, arterial punctures, contrast associated nephropathy, bleeding complications, and large costs. The accuracy of interpretation by both computer algorithm identification and amongst expert clinicians, including cardiologists, shows that it has low specificity and sensitivity to be useful in diagnosing ACO [40]. In addition, reliance on computer interpretation can miss many dynamic changes and other morphologies indicative of ACO, yet clinicians often find readings of “Normal” as a reassuring sign. It is often on next day angiography that NSTEMI patients with ACO are discovered, which leads to almost double short- and long-term mortality compared to NSTEMI patients without occlusion [13]. It is clear that the STEMI/NSTEMI paradigm is inaccurate in diagnosing ACO, and detrimental to the NSTEMI patients with ACO that are routinely missed.

As a cognitive roadblock the STEMI/NSTEMI paradigm continues to undermine progress in several ways. It presents itself in a way that makes one think that STE on ECG is the most important marker of ACO, disregarding any other potential ECG findings that investigators have found to be indicative of ACO with high accuracy [51]. Furthermore, when the ECG is non-diagnostic, focus on other clinical, laboratory, and imaging findings can be valuable in determining high risk individuals needing emergent reperfusion, but current guidelines simply fail to emphasize the use of them [51,72]. Classifying patients based on a surrogate marker, which STEMI/NSTEMI does, misses the underlying pathology of acute coronary occlusion, and misses the bigger picture of what needs to be determined clinically; who needs emergent reperfusion therapy and who does not? Improvements via retrospective analysis to improve ACO discovery is also rather difficult under the current paradigm since we are taught lack of STE is a reassuring sign, disregard the harms in missing STEMI (-) OMI patients, and group NSTEMI patients as one homogenous group even when ACO is discovered later in the clinical course.

OMI/NOMI as a Better Paradigm

To improve outcomes in patients with ACO the underlying pathology must be the center of a paradigm. OMI/NOMI is an emerging paradigm that can do that, by OMI conceptually equating to as an acute coronary occlusion or near occlusion with insufficient collateral circulation, such that downstream myocardium will undergo imminent infarction without timely reperfusion. OMI emphasizes the underlying pathology and so in return utilizes all diagnostic factors including many other ECG findings, biomarkers, echocardiography, computed tomography, or conventional angiography [51].

It has been shown that the OMI/NOMI approach using other ECG findings indicative of ACO compared to STEMI/NSTEMI criteria results in more accurate diagnosis of ACO [74-75].

Comparing STEMI (-) OMI patients to STEMI (+) OMI patients shows similar infarct sizes and mortality risks, yet delayed time to angiography. With the OMI/NOMI approach earlier diagnosis of ACO was achieved in 55% of the OMI cohort on average 3 hours earlier and a median of 1.5 hours than using the STEMI/NSTEMI model [75]. It is also evident that ECG interpretation can be improved upon through educational feedback programs for emergency physicians, which has shown to decrease cath lab activation time with more accurate interventions [48]. Taking the current literature together suggests that ultimately using the OMI/NOMI model leads to a more accurate and timely diagnosis in patients presenting with potential ACO, leading to earlier definitive intervention and thus improved mortality and morbidity outcomes.

Limitations

Limitations of the research on OMI/NOMI compared to STEMI/NSTEMI exist. The research directly comparing the two paradigms were primarily retrospective which can create bias, external validity issues, and long term follow up data difficult to generalize. One of the bigger limitations is that a randomized clinical trial of immediate vs. delayed angiography is needed to determine if STEMI (-) OMI patients would indeed undergo earlier intervention than STEMI (+) OMI patients and have improved outcomes. With OMI/NOMI paradigm and proposed algorithm still showed 17.9% of ACO is missed [10]. However, by moving to a paradigm that is more open to discovering new ECG findings and utilizing other factors indicative of ACO, that number will likely go down. ECG interpretation is subjective and requires experience for accurate interpretation. The subtleties and complexities associated with the other ECG findings suggestive of ACO will likely make the OMI/NOMI approach more difficult to novice interpreters. Furthermore, ECG findings need to be interpreted in the clinical

context as well. But it has also been shown that clinicians can adapt and broaden their ECG understanding to improve diagnosis ability [48]. By instituting the OMI/NOMI paradigm potentially new trials can be performed, the research can be furthered, and ultimately patients can benefit in the long run. Indeed, future results are always contingent on parameters outside merely diagnosing ACO, and improvements in factors such as revascularization procedures and post cardiac rehabilitation will be vital in treating patients and improving outcomes as well.

Conclusion:

ACS continues to be a significant proportion of patients presenting to emergency department, yet our current dichotomous STEMI/NSTEMI paradigm fails to adequately capture all of the patients requiring emergent reperfusion therapy. Examining the historical context in which STEMI/NSTEMI was developed reveals flawed methodology that has nevertheless led to it becoming the dogmatic approach to determining who has ACO requiring emergent reperfusion therapy. Furthermore, as a paradigm it fails to progress the knowledge of ACO and hinders a substantial amount of ACS patients from receiving definitive treatment. With nearly 30% of NSTEMI patients having totally occluded coronary arteries determined on delayed angiography the need for a paradigm shift to capture these patients is required to improve outcomes. Focusing on an ECG surrogate marker of ACO fails to consider the underlying pathophysiology. The OMI/NOMI paradigm is more inclusive of other ECG findings shown to be highly accurate indicators of ACO, as well as use of echocardiography, biomarkers, computed tomography, and conventional angiography. When the OMI/NOMI paradigm approach of ECG interpretation was compared to STEMI/NSTEMI, earlier and more accurate diagnosis was made. Furthermore, when other ACO indicative ECG findings under the OMI/NOMI model were taught to emergency physicians, cath lab activation was faster and more accurate supporting its usefulness

as a model. The findings presented in this paper suggest the OMI/NOMI paradigm can successfully improve outcomes in patients presenting to the ED with ACS, but future randomized clinical trials are needed to answer that question more definitively.

References

1. Smith JN, Negrelli JM, Manek MB, Hawes EM, Viera AJ. Diagnosis and Management of Acute Coronary Syndrome: An Evidence-Based Update. The Journal of the American Board of Family Medicine. 2015;28(2):283-293. doi:10.3122/jabfm.2015.02.140189

2. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy insuspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet. 1994 Feb 5;343(8893):311-22.

3. Menown et al. Optimizing the initial 12-lead electrocardiographic diagnosis of acute myocardial infarction. European Heart J. 2000 Feb;21(4):275-83. (PMID: 10653675)

4. Macfarlane et al. Age, sex, and the ST amplitude in health and disease. J Electrocardiol. 2001;34 Suppl:235-41. (PMID:11781962)

5. J.P. Collet et al., ESC Scientific Document Group, 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC), Eur. Heart J., Volume 42, Issue 14, 7 April 2021, Pages 1289–1367, https://doi.org/10.1093/eurheartj/ehaa575

6. Khan AR, Golwala H, Tripathi A, et al. Impact of total occlusion of culprit artery in acute non-ST elevation myocardial infarction: a systematic review and meta-analysis. Eur Heart J. 2017;38(41):3082-3089. doi:10.1093/eurheartj/ehx418

7. Hung CS, Chen YH, Huang CC, et al. Prevalence and outcome of patients with non-ST segment elevation myocardial infarction with occluded "culprit" artery - a systemic review and meta-analysis. Crit Care. 2018;22(1):34. Published 2018 Feb 9. doi:10.1186/s13054-018-1944-x

8. Fuster V, Kovacic JC. Acute coronary syndromes: pathology, diagnosis, genetics, prevention, and treatment. Circ Res. 2014;114(12):1847-1851. doi:10.1161/CIRCRESAHA.114.302806

9. Basit H, Malik A, Huecker MR. Non ST Segment Elevation Myocardial Infarction. [Updated 2021 Apr 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls

10. Aslanger EK, Yıldırımtürk Ö, Şimşek B, et al. DIagnostic accuracy oF electrocardiogram for acute coronary OCClUsion resuLTing in myocardial infarction (DIFOCCULT Study). Int J Cardiol Heart Vasc. 2020;30:100603. Published 2020 Jul 30. doi:10.1016/j.ijcha.2020.100603

11. B. Ibanez, et al. ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the task force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC) Eur. Heart J., 39 (2018), pp. 119-177

12. DeWood MA, Spores J, Notske R, et al. Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. The New England Journal of Medicine. 1980;303(16):897-902. doi:10.1056/NEJM198010163031601

13. Khan AR, Golwala H, Tripathi A, et al. Impact of total occlusion of culprit artery in acute non-ST elevation myocardial infarction: a systematic review and meta-analysis. Eur Heart J. 2017;38(41):3082-3089. doi:10.1093/eurheartj/ehx418

14. Cohen M, Visveswaran G. Defining and managing patients with non-ST-elevation myocardial infarction: Sorting through type 1 vs other types. Clin Cardiol. 2020;43(3):242-250. doi:10.1002/clc.23308

15. Avci BK, Ikitimur B, Tok OO, et al. The role of GRACE score in the prediction of high-risk coronary anatomy in patients with non-ST elevation acute coronary syndrome. Kardiol Pol. 2015;73(8):592-597. doi:10.5603/KP.a2015.0030

16. Committee Members, Ryan TJ, Anderson JL, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction. Journal of the American College of Cardiology. 1996;28(5):1328-1419. doi:10.1016/s0735-1097(96)00392-0

17. Aslanger EK, Meyers HP, Smith SW. Time for a new paradigm shift in myocardial infarction. The Anatolian Journal of Cardiology. 2021;25(3):156-162. doi:10.5152/anatoljcardiol.2021.89304

18. Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI) Lancet. 1986;1:397–402.

19. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. The Lancet. 1996;348(9030):771-775. doi:10.1016/S0140-6736(96)02514-7

20. Braunwald et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol. 2000 Sep;36(3):970-1062.

21. Alpert et al. Myocardial infarction redefined - a consensus document of The Joint European

22. Wu et al. Normal limits of the electrocardiogram in Chinese subjects. Int J Cardiol. 2003 Jan;87(1):37-51.

23. Antman et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction - executive summary. A report of the American College of Cardiology/American Heart Association task force on practice guidelines. J Am Coll Cardiol. 2004 Aug 4;44(3):671-719.

24. Macfarlane et al. Modification of ACC/ESC criteria for acute myocardial infarction. J Electrocardiol. 2004;37 Suppl:98-103. (PMID: 15534817)

25. Thygesen et al. Universal definition of myocardial infarction. Joint ESC/ACCF/AHA/WHF task force for the redefinition of myocardial infarction. J Am Coll Cardiol. 2007 Nov 27;50(22):2173-95. (PMID: 18036459)

26. Wagner et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction. J Am Coll Cardiol. 2009 Mar 17;53(11):1003-11. (PMID: 19281933)

27. Thygesen et al. Third universal definition of myocardial infarction. J Am Coll Cardiol. 2012 Oct 16;60(16):1581-98. (PMID: 22958960)

28. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). Journal of the American College of Cardiology. 2018;72(18):2231-2264. doi:10.1016/j.jacc.2018.08.1038

29. Schmitt et al. Diagnosis of acute myocardial infarction in angiographically documented occluded infarct vessel: limitations of ST-segment elevation in standard and extended ECG leads. Chest. 2001 Nov;120(5):1540-6. (PMID: 11713132)

30. Wang et al. Incidence, distribution, and prognostic impact of occluded culprit arteries among patients with non-ST-elevation acute coronary syndromes undergoing diagnostic angiography. Am Heart J. 2009 Apr;157(4):716-23.

31. Pride et al. Angiographic and clinical outcomes among patients with acute coronary syndromes presenting with isolated anterior ST-segment depressions. JACC Cardiovasc Interv. 2010 Aug;3(8):806-11.

32. Khan et al. Impact of total occlusion of culprit artery in acute non-ST elevation myocardial infarction: a systematic review and meta-analysis. European Heart J, 2007. 38, 3082-3089.

33. Marti D et al. Incidence, angiographic features, and outcomes of patient presenting with subtle ST-elevation myocardial infarction. Am Heart J 2014; 168:884-90.

34. Smith et al. Electrocardiographic differentiation of early repolarization from subtle anterior ST-segment elevation myocardial infarction. Ann Emerg Med. 2012;60:45-56.

35. From AM et al. Acute myocardial infarction due to left circumflex artery occlusion and significance of ST-segment elevation. The American journal of cardiology 2010;106:1081-5.

36. McCabe et al. Physician accuracy in interpreting potential ST-segment elevation myocardial infarction electrocardiograms. Journal of the American Heart Association 2013;2:e000268.

37. Jayroe et al. Differentiating ST elevation myocardial infarction and nonischemic causes of ST elevation by analyzing the presenting electrocardiogram. The American Journal of Cardiology 2009;103:301-6.

38. Tran et al. Differentiating ST-elevation myocardial infarction from nonischemic ST-elevation in patients with chest pain. The American journal of cardiology 2011;108:1096-101.

39. Carley et al. What's the point of ST elevation? Emerg Med J. 2002;19:126-128.

40. Hillinger P, Strebel I, Abächerli R, et al. Prospective validation of current quantitative electrocardiographic criteria for ST-elevation myocardial infarction. Int J Cardiol. 2019;292:1-12. doi:10.1016/j.ijcard.2019.04.041

41. McCabe et al. Prevalence and factors associated with false-positive ST-segment elevation myocardial infarction diagnoses at primary percutaneous coronary intervention-capable centers: a report from the Activate-SF registry. Arch Intern Med. 2012;172:864–871.

42. Larson et al. "False-positive" cardiac catheterization laboratory activation among patients with suspected ST-segment elevation myocardial infarction. JAMA. 2007;298:2754–2760.

43. Schläpfer J, Wellens HJ. Computer-Interpreted Electrocardiograms: Benefits and Limitations. Journal of the American College of Cardiology. 2017;70(9):1183-1192. doi:10.1016/j.jacc.2017.07.723

44. Mawri S, Michaels A, Gibbs J, et al. The Comparison of Physician to Computer Interpreted Electrocardiograms on ST-elevation Myocardial Infarction Door-to-balloon Times. Critical Pathways in Cardiology. 2016;15(1):22-25. doi:10.1097/hpc.0000000000000067

45. Garvey JL, Zegre-Hemsey J, Gregg R, Studnek JR. Electrocardiographic diagnosis of ST segment elevation myocardial infarction: An evaluation of three automated interpretation algorithms. Journal of Electrocardiology. 2016;49(5):728-732. doi:10.1016/j.jelectrocard.2016.04.010

46. O'Connor RE, Al Ali AS, Brady WJ, et al. Part 9: Acute Coronary Syndromes. Circulation. 2015;132(18 suppl 2):S483-S500. doi:10.1161/cir.0000000000000263

47. Martínez-Losas P, Higueras J, Gómez-Polo JC, et al. The influence of computerized interpretation of an electrocardiogram reading. The American Journal of Emergency Medicine. 2016;34(10):2031-2032. doi:10.1016/j.ajem.2016.07.029

48. McLaren JTT, Taher AK, Kapoor M, Yi SL, Chartier LB. Sharing and Teaching Electrocardiograms to Minimize Infarction (STEMI): reducing diagnostic time for acute coronary occlusion in the emergency department. The American Journal of Emergency Medicine. 2021;48:18-32. doi:10.1016/j.ajem.2021.03.067

49. Litell JM, Meyers HP, Smith SW. Emergency physicians should be shown all triage ECGs, even those with a computer interpretation of "Normal." Journal of Electrocardiology. 2019;54:79-81. doi:10.1016/j.jelectrocard.2019.03.003

50. Aslanger EK, Meyers PH, Smith SW. STEMI: A transitional fossil in MI classification?. J Electrocardiol. 2021;65:163-169. doi:10.1016/j.jelectrocard.2021.02.001

51. Tziakas D, Chalikias G, Al-Lamee R, Kaski JC. Total coronary occlusion in non ST elevation myocardial infarction: Time to change our practice? International Journal of Cardiology. 2021;329:1-8. doi:10.1016/j.ijcard.2020.12.082

52. Driver BE, Khalil A, Henry T, Kazmi F, Adil A, Smith SW. A new 4-variable formula to differentiate normal variant ST segment elevation in V2-V4 (early repolarization) from subtle left anterior descending coronary occlusion - Adding QRS amplitude of V2 improves the model. J Electrocardiol. 2017;50(5):561-569. doi:10.1016/j.jelectrocard.2017.04.005

53. Aslanger E, Yıldırımtürk Ö, Bozbeyoğlu E, et al. A Simplified Formula Discriminating Subtle Anterior Wall Myocardial Infarction from Normal Variant ST-Segment Elevation. Am J Cardiol. 2018;122(8):1303-1309. doi:10.1016/j.amjcard.2018.06.053

54. Lee et al. Terminal QRS distortion is present in anterior myocardial infarction but absent in early repolarization. Am J Emerg Med 2016;34:2182-5.

55. Y. BIRNBAUM, S. SCLAROVSKY, A. MAGER, B. STRASBERG, E. RECHAVIA, ST segment depression in aVL: a sensitive marker for acute inferior myocardial infarction, European Heart Journal, Volume 14, Issue 1, January 1993, Pages 4–7, https://doi.org/10.1093/eurheartj/14.1.4

56. Bischof et al. ST depression in lead aVL differentiates inferior ST-elevation myocardial infarction from pericarditis. Am J Emerg Med 2016;34:149-54.

57. Smith SW, Dodd KW, Henry TD, Dvorak DM, Pearce LA. Diagnosis of ST-elevation myocardial infarction in the presence of left bundle branch block with the ST-elevation to S-wave ratio in a modified Sgarbossa rule [published correction appears in Ann Emerg Med. 2013 Oct;62(4):302]. Ann Emerg Med. 2012;60(6):766-776. doi:10.1016/j.annemergmed.2012.07.119

58. Mitchell GJ, Dodd K, Zvosec DL, et al. P103: Performance characteristics of the modified Sgarbossa criteria for diagnosis of acute coronary occlusion in emergency department patients with ventricular paced rhythm and symptoms of acute coronary syndrome. CJEM. 2018;20(S1):S93-S93. doi:10.1017/cem.2018.301

59. E.J. Armstrong, A.R. Kulkarni, P.D. Bhave, et al. Electrocardiographic criteria for ST-elevation myocardial infarction in patients with left ventricular hypertrophy Am J Cardiol, 110 (2012), pp. 977-983

60. L.R. Klein, G.R. Shroff, W. Beeman, S.W. Smith Electrocardiographic criteria to differentiate acute anterior ST-elevation myocardial infarction from left ventricular aneurysm Am J Emerg Med, 33 (2015), pp. 786-790

61. J.E. Bischof, C. Worrall, P. Thompson, D. Marti, S.W. Smith ST depression in lead aVL differentiates inferior ST-elevation myocardial infarction from pericarditis Am J Emerg Med, 34 (2016), pp. 149-154

62. Shaikh S, Al-Sadawi M, Dogar MU, et al. New Onset Right Bundle Branch Block In Acute Coronary Syndrome and High-Grade Stenosis: A Case Series. Scifed J Cardiol. 2019;3(1):23.]

63. Aslanger E, Yıldırımtürk Ö, Şimşek B, et al. A new electrocardiographic pattern indicating inferior myocardial infarction. Journal of Electrocardiology. 2020;61:41-46. doi:10.1016/j.jelectrocard.2020.04.008

64. G Rajendran, S Mahalingam, R Kagne, B Nathan, The South African flag sign—an electrocardiographic sign to predict the culprit artery, QJM: An International Journal of Medicine, 2021;, hcab137, https://doi.org/10.1093/qjmed/hcab137

65. Collins MS, Carter JE, Dougherty JM, Majercik SM, Hodsden JE, Logue EE. Hyperacute T-wave criteria using computer ECG analysis. Ann Emerg Med. 1990;19(2):114-120. doi:10.1016/s0196-0644(05)81792-5

66. Morris NP, Body R. The De Winter ECG pattern: morphology and accuracy for diagnosing acute coronary occlusion: systematic review. Eur J Emerg Med. 2017;24(4):236-242. doi:10.1097/MEJ.0000000000000463

67. Miner B, Grigg WS, Hart EH. Wellens Syndrome. [Updated 2020 Aug 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482490/]

68. Cipriani A, D'Amico G, Brunello G, et al. The electrocardiographic "triangular QRS-ST-T waveform" pattern in patients with ST-segment elevation myocardial infarction: Incidence, pathophysiology and clinical implications. J Electrocardiol. 2018;51(1):8-14. doi:10.1016/j.jelectrocard.2017.08.023

69. Miranda DF, Lobo AS, Walsh B, Sandoval Y, Smith SW. New Insights Into the Use of the 12-Lead Electrocardiogram for Diagnosing Acute Myocardial Infarction in the Emergency Department. Canadian Journal of Cardiology. 2018;34(2):132-145. doi:10.1016/j.cjca.2017.11.011

70. Beller GA. Myocardial perfusion imaging for detection of silent myocardial ischemia. Am J Cardiol. 1988;61(12):22F-28F. doi:10.1016/0002-9149(88)90051-3

71. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130:2354.

72. Grenne B, Eek C, Sjøli B, et al. Acute coronary occlusion in non-ST-elevation acute coronary syndrome: outcome and early identification by strain echocardiography. Heart. 2010;96(19):1550-1556. doi:10.1136/hrt.2009.188391

73. Sankardas MA, Ramakumar V, Farooqui FA. Of Occlusions, Inclusions, and Exclusions: Time to Reclassify Infarctions? Circulation. 2021;144(5):333-335. doi:10.1161/circulationaha.121.055827

74. Meyers HP, Bracey A, Lee D, et al. Comparison of the ST-Elevation Myocardial Infarction (STEMI) vs. NSTEMI and Occlusion MI (OMI) vs. NOMI Paradigms of Acute MI. J Emerg Med. 2021;60(3):273-284. doi:10.1016/j.jemermed.2020.10.026

75. Pendell Meyers H, Bracey A, Lee D, et al. Accuracy of OMI ECG findings versus STEMI criteria for diagnosis of acute coronary occlusion myocardial infarction. IJC Heart & Vasculature. 2021;33:100767. doi:10.1016/j.ijcha.2021.100767

76. Aslanger EK, Yıldırımtürk Ö, Şimşek B, et al. DIagnostic accuracy oF electrocardiogram for acute coronary OCClUsion resuLTing in myocardial infarction (DIFOCCULT Study). Int J Cardiol Heart Vasc. 2020;30:100603. Published 2020 Jul 30. doi:10.1016/j.ijcha.2020.100603

Appendix

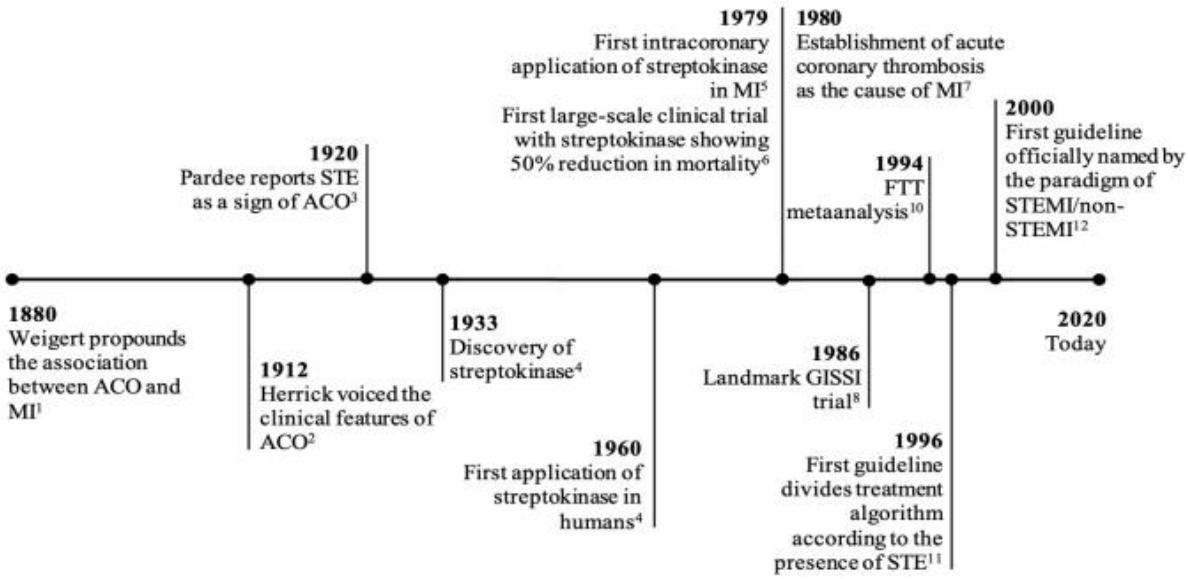


Figure 1. A timeline of major events providing insights into the acute myocardial infarction pathogenesis and management [17].

Table 1. Electrocardiographic signs indicative of non-ST elevation myocardial infarction with total occlusion of the culprit coronary artery [51].

Non-coronary specific signs
Total number of leads showing ST-segment depression (>3)
Total ST-segment depression sum (≥ 6 mm)
ST-segment depression > 2 mm in any lead
Presence of q waves in ≥ 2 contiguous leads
Hyperacute T waves
'Shark-fin' – triangular waveform ECG pattern
Transient ST-segment elevation
Low QRS voltage
LAD specific signs
Hyperacute T waves
De Winter's sign
Wellens' sign (Type A & Type B)
'Shark-fin' – triangular waveform ECG pattern
New RBBB
Resting U-wave inversion
LCx specific signs
ST-segment depression and/or T-wave inversion in inferolateral leads
ST-segment depression in V_1-V_3 leads
ST-segment elevation in V_7-V_8 leads
Prominent R-waves in V_1-V_2 (R/S > 1) with upright T waves V_1-V_3
RCA specific signs
ST-segment depression and/or T-wave inversion in inferolateral leads
ST-segment depression in V_1-V_3 leads
ST-segment elevation in V_7-V_8 leads
Prominent R-waves in V_1-V_2 (R/S > 1) with upright T waves V_1-V_3
ST-segment elevation in lead $V4_R$
ST-segment elevation in lead V_1

Deep ST-segment depression in lateral leads (I + aVL ≥ 2 mm & ST depression aVL > I)
QRS prolongation or epsilon wave in lead $V4_R$
LM specific signs
ST-segment elevation in aVR lead
ST-segment depression in all leads
ST-elevation in lead aVR ≥V_1
'Shark-fin' – triangular waveform ECG pattern
Other high-risk signs
New RBBB
Myocardial infarction on previous LBBB using Scarbossa criteria
AV conduction abnormalities

AV; atrioventricular, ECG; electrocardiogram, LBBB; left bundle branch block, RBBB, right bundle branch block.
New LBBB is considered as STEMI by definition and requires urgent coronary angiography.

Figure 2. Left anterior descending coronary artery ECG specific signs [51]

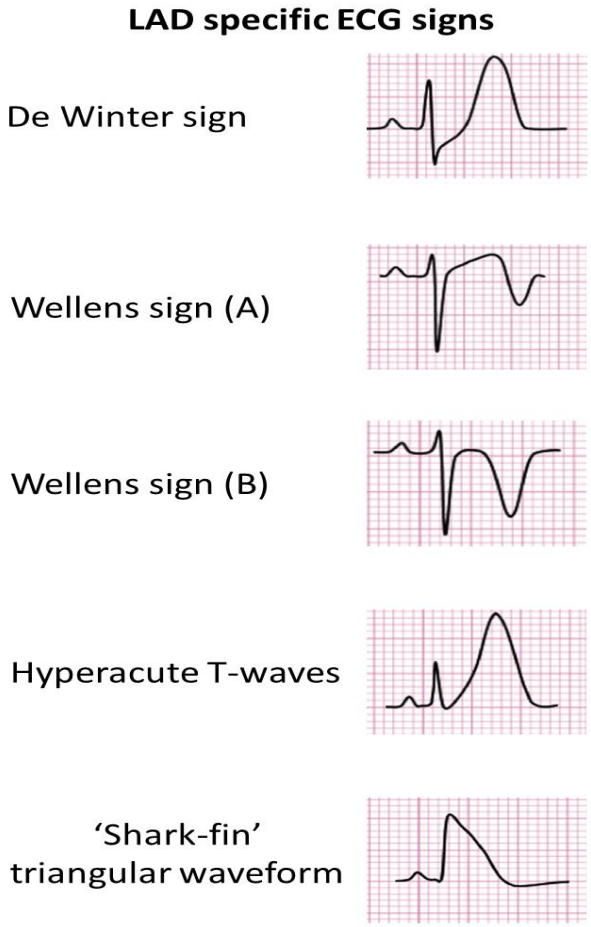


Figure 3. Left circumflex coronary artery ECG specific signs [51]

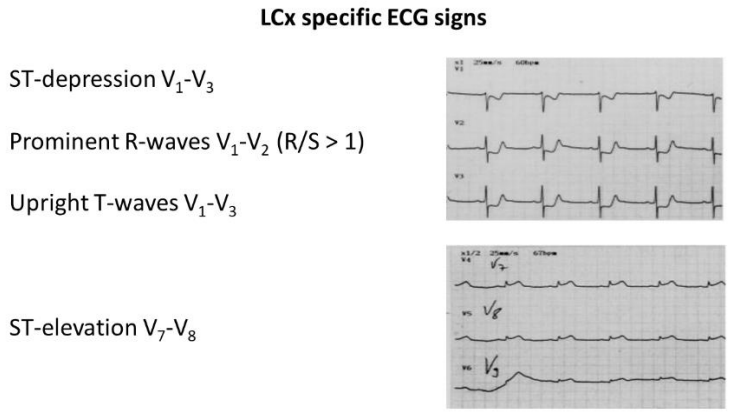


Figure 4. Right coronary artery ECG specific signs [51]

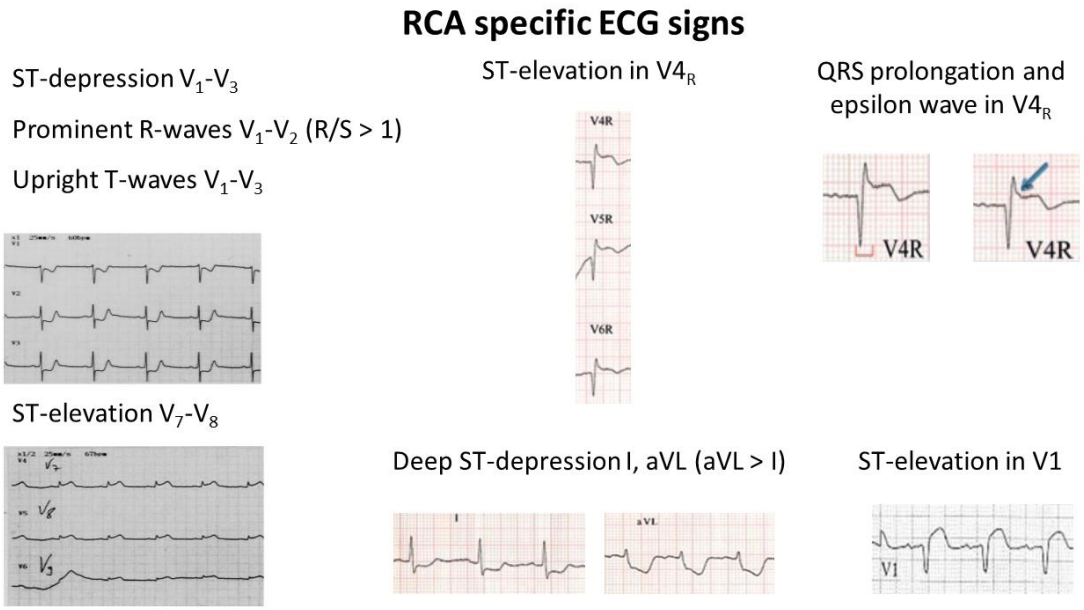
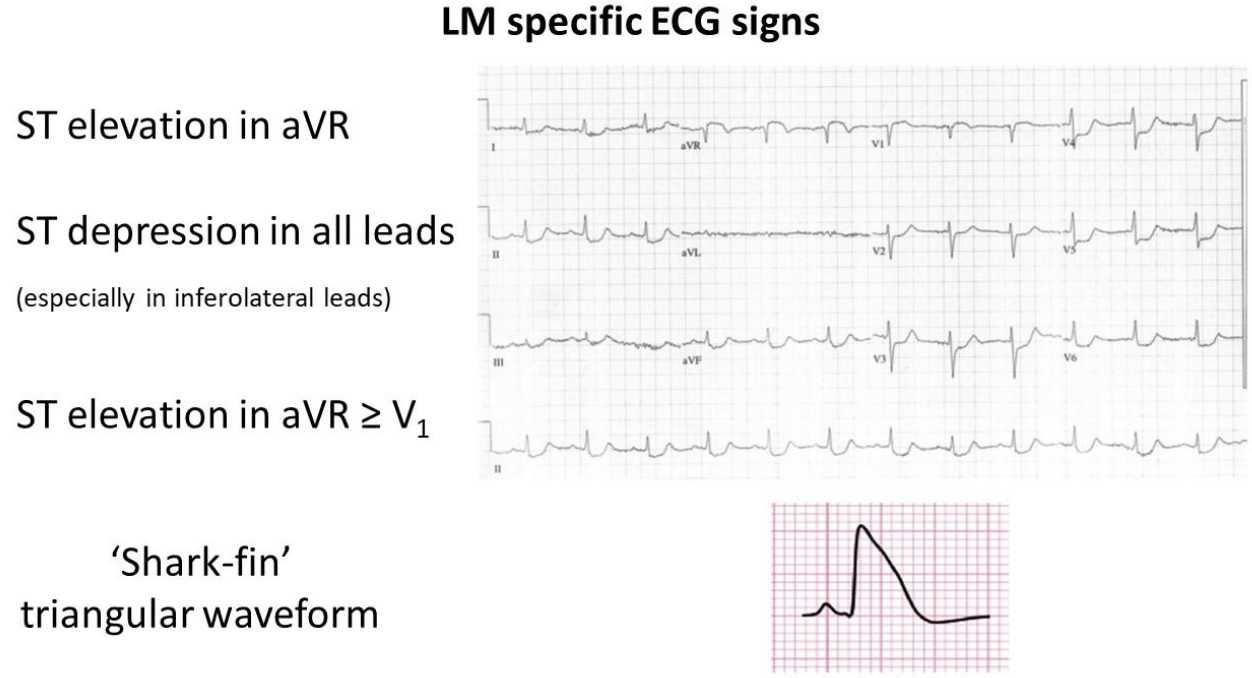


Figure 5. Left main coronary artery ECG specific signs [51]



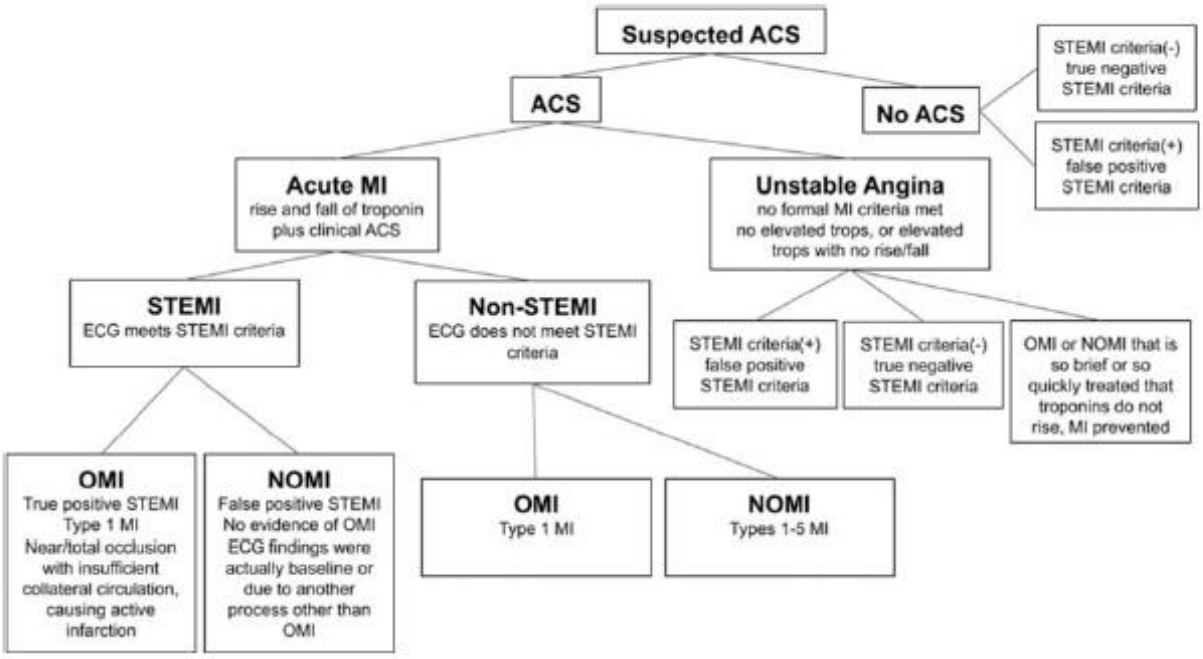


Figure 6. The acute coronary syndrome (ACS) spectrum using the ST-segment elevation myocardial infarction (STEMI) vs. non-STEMI paradigm primarily. The current paradigm of MI divides acute MI into STEMI and non-STEMI based on the electrocardiogram (ECG). Occlusion myocardial infarction (OMI) and nonocclusion myocardial infarction (NOMI) are possible in both STEMI and non-STEMI categories. [74]

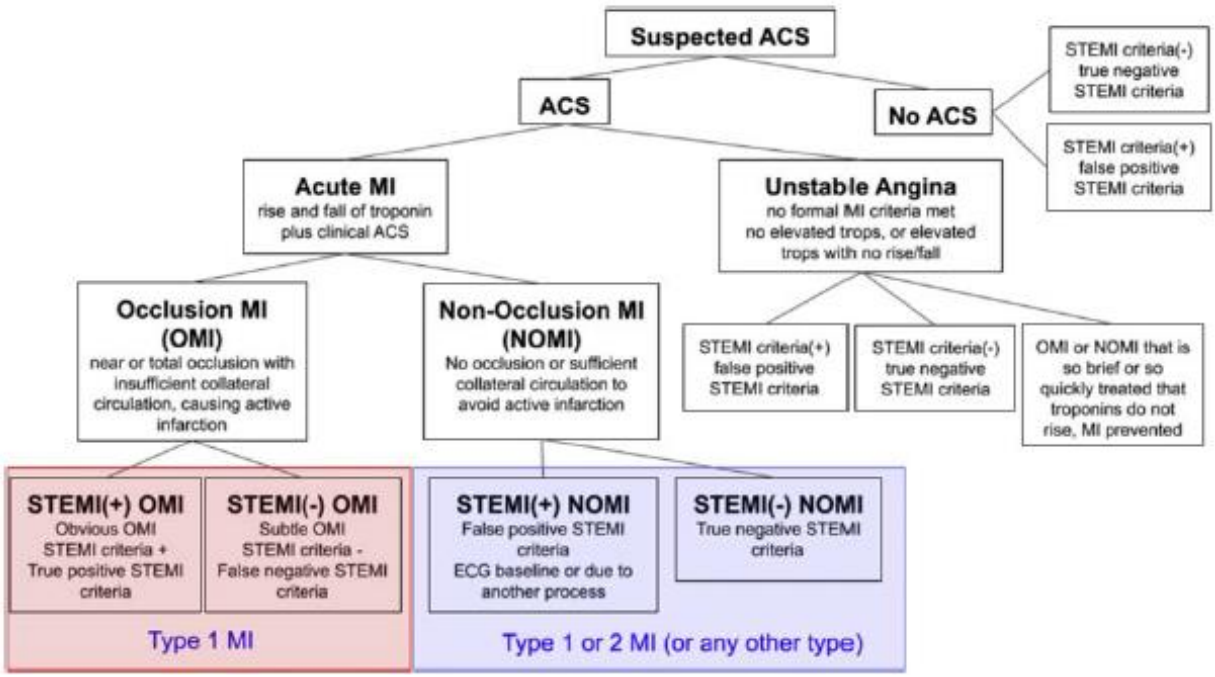


Figure 7. The acute coronary syndrome (ACS) spectrum using the occlusion myocardial infarction (OMI) vs. nonocclusion myocardial infarction (NOMI) paradigm primarily. The proposed paradigm of MI divides acute MI into OMI and NOMI. OMI are those for whom thrombolytics and percutaneous coronary intervention were conceptually designed and indicated, but many OMI do not manifest ST-segment elevation myocardial infarction (STEMI) criteria. ECG = electrocardiogram. [74]

AUGSBURG
UNIVERSITY

Augsburg University Institutional Repository Deposit Agreement

By depositing this Content ("Content") in the Augsburg University Institutional Repository known as Idun, I agree that I am solely responsible for any consequences of uploading this Content to Idun and making it publicly available, and I represent and warrant that:

- I am *either* the sole creator or the owner of the copyrights in the Content; or, without obtaining another's permission, I have the right to deposit the Content in an archive such as Idun.
- To the extent that any portions of the Content are not my own creation, they are used with the copyright holder's expressed permission or as permitted by law. Additionally, the Content does not infringe the copyrights or other intellectual property rights of another, nor does the Content violate any laws or another's right of privacy or publicity.
- The Content contains no restricted, private, confidential, or otherwise protected data or information that should not be publicly shared.

I understand that Augsburg University will do its best to provide perpetual access to my Content. To support these efforts, I grant the Board of Regents of Augsburg University, through its library, the following non-exclusive, perpetual, royalty free, worldwide rights and licenses:

- To access, reproduce, distribute and publicly display the Content, in whole or in part, to secure, preserve and make it publicly available
- To make derivative works based upon the Content in order to migrate to other media or formats, or to preserve its public access.

These terms do not transfer ownership of the copyright(s) in the Content. These terms only grant to Augsburg University the limited license outlined above.

Initial one:

IT I agree and I wish this Content to be Open Access.

___ I agree, but I wish to restrict access of this Content to the Augsburg University network.

Work (s) to be deposited

Title: Does Transitioning to an OMI/NOMI Model for the Evaluation of Acute Coronary Syndrome in Adult Emergency department Patients Improve Outcomes Compared to Contemporary STEMI/NSTEMI Model?

Author(s) of Work(s): Ismar Terzic

Depositor's Name (Please Print): Alicia Quella

Author's Signature: Ismar Terzic Date: 08/16/2021

If the Deposit Agreement is executed by the Author's Representative, the Representative shall separately execute the following representation.

I represent that I am authorized by the Author to execute this Deposit Agreement on the behalf of the Author.

Author's Representative Signature: _____ Date: _____